Antimicrobial Shortages
Role of the CEC

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Clinical Excellence Commission

NSW AMS Forum – August 2017

The Problem

- Increase in:
  - Number of drugs affected by shortages
  - Number of antimicrobial shortages
  - Number of shortages involving parenteral formulations
  - Duration of shortages
  - Resources and cost to manage shortages

- Impact to patients:
  - Care may be compromised, delayed or completely prevented
  - Suboptimal and delayed therapy for serious infectious diseases can compromise patient safety and result in poorer outcomes, including death
  - Possible harm due to unexpected or unmanageable side effects of alternative
  - Increased risk of harm from medication errors due to use of unfamiliar alternative

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Scope of antimicrobial problem

- In the USA:
  - 148 antibiotics experienced shortages between 2001 and 2013[1]
  - 46% of those antibiotics are used to treat high-risk pathogens, including *C. difficile*, CRE, MRSA, and *Pseudomonas aeruginosa*[1]
  - Antimicrobial drugs account for 13% of all drugs in short supply, second only to chemotherapeutic drugs[2]
  - Between 2006 and 2010, antimicrobial drug shortages increased by 283%[2]

1. Quadri, F., et al., *Antibacterial Drug Shortages From 2001 to 2013: Implications for Clinical Practice.* Clinical Infectious Diseases, 2015.
2. Borchardt, R.A. and K.V. Rolston, *Antibiotic shortages: effective alternatives in the face of a growing problem.* JAAPA, 2013. **26**(2): p. 13, 18.

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Reason for shortage = complex

- Increased global reliance on single manufacturers for active ingredients
- Manufacturing issues
- Discontinuation of a medicine
- Increased demand
- Regulatory issues
- Recalls
- Economic decision remove from market

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Managing shortages

- National
  - Therapeutic Goods Administration
    - Medicine Shortages Information Initiative
    - Regulation of Special Access Scheme and Section 19A
  - National Medication Shortage Working Party
- State
  - Strategic Procurement Services, HealthShare (contract items)
  - Model for Multi-Agency Management of Medication Shortages in NSW
- Local
  - Sponsors (manufacturers)
  - Wholesalers
  - Pharmacies

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Communication of shortages

- Model for Multi-Agency Management of Medication Shortages in NSW
  - Proposed in February 2014
  - Agreed in March 2014
  - Commenced in April 2014
- Continually revising
  - Best mechanism for distribution
  - Process for low risk medication shortages
  - Is it working?

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Model for multi-agency management of medication shortages in NSW

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Agencies involved

Members of the Medicines Shortage Assessment and Management Team:

- The Office of the Chief Health Officer
- Chief Pharmacist Unit, Legal and Regulatory Services Branch
- Strategic Procurement Services, HealthShare
- Clinical Excellence Commission

Information gathering and communication:

- Expert Clinicians in the relevant field
- CEC AMS Expert Advisory Committee
- Clinical Networks, Agency of Clinical Innovation
- NSW Therapeutic Advisory Group and members
- Chief Executives and Directors of Clinical Governance

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Information gathering

- Receive notification of a shortage
  - Not all shortages are notified
  - Various sources
- Investigate details of shortage
  - The specific product in short supply
  - Expected duration of the shortage
  - Any action that has already been taken or communication that has been disseminated

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Risk assessment

- Details of shortage or potential shortage
- Availability of alternative products
    1. Registered products
    2. Non-registered products
- Risk associated with the unavailability of a medicine
- Risk associated with replacement medicines

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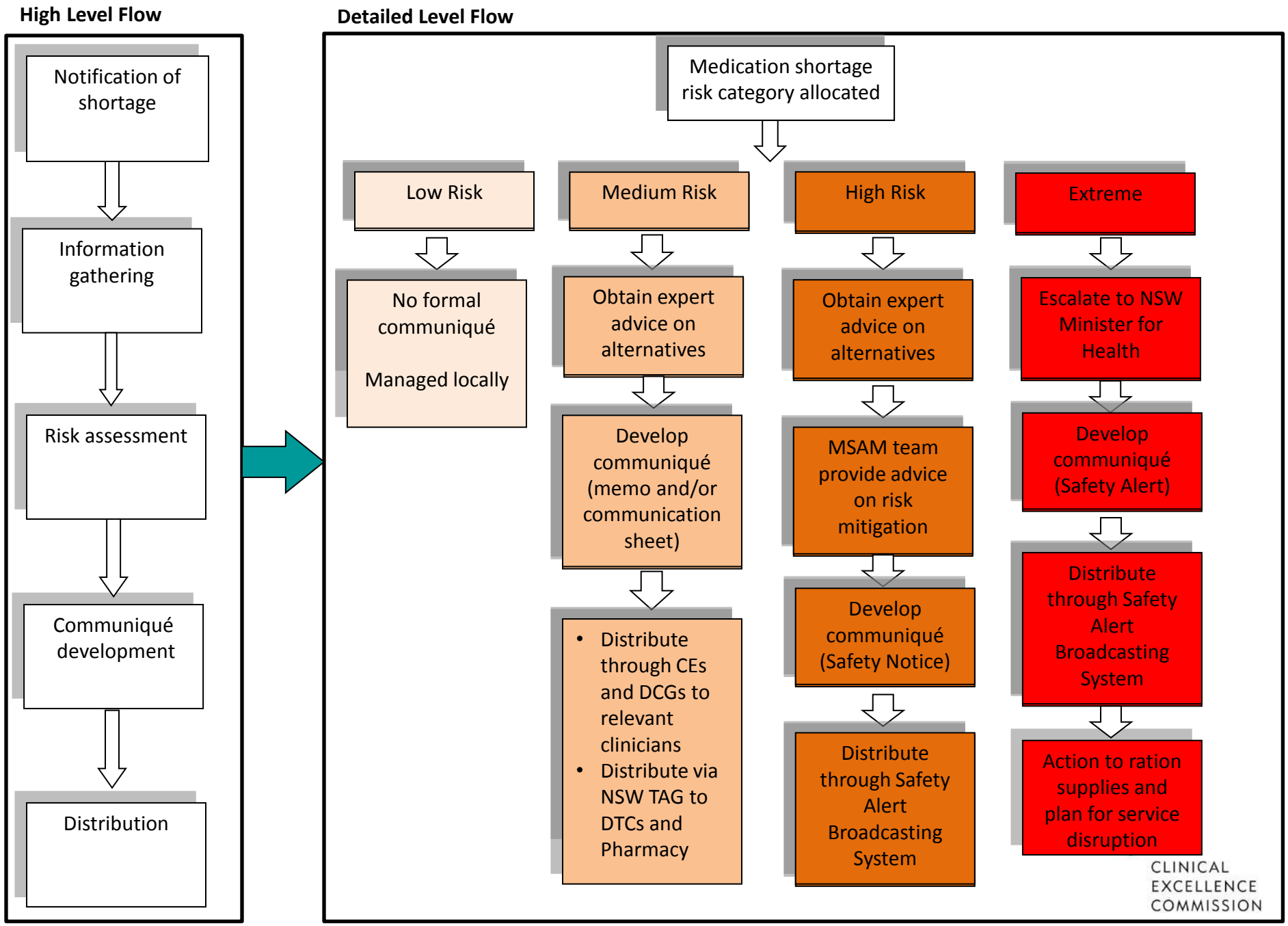
Antimicrobial	Uses and alternatives
IV aciclovir	*Use:* serious HSV/VZV infections (e.g. herpes simplex encephalitis, opthalmic herpes zoster, neonatal HSV) *Alternative agents:* ganciclovir, foscarnet & cidofovir *Risk associated with alternatives:* • Ganciclovir – bone marrow suppression • Foscarnet – decreased renal function and electrolyte abnormalities • Cidofovir – nephrotoxicity
IV vancomycin	*Use:* Gram-positive bacterial infections suspected or known to be resistant to first-line antibiotics *Alternative agents:* teicoplanin, daptomycin, linezolid & ceftaroline *Risk associated with alternatives:* • Teicoplanin – similar to vancomycin • Daptomycin – increase CK • Linezolid – myelosuppression, optic and peripheral neuropathy • Ceftaroline – neutropenia if treated > 2-3 weeks


High Level Flow
Notification of shortage
Information gathering
Risk assessment
Communiqué development
Distribution
Detailed Level Flow
Medication shortage risk category allocated
Low Risk
No formal communiqué
Managed locally
Medium Risk
Obtain expert advice on alternatives
Develop communiqué (memo and/or communication sheet)
Distribute through CEs and DCGs to relevant clinicians
Distribute via NSW TAG to DTCs and Pharmacy
High Risk
Obtain expert advice on alternatives
MSAM team provide advice on risk mitigation
Develop communiqué (Safety Notice)
Distribute through Safety Alert Broadcasting System
Extreme
Escalate to NSW Minister for Health
Develop communiqué (Safety Alert)
Distribute through Safety Alert Broadcasting System
Action to ration supplies and plan for service disruption
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Risk mitigation strategies

- Source alternative product
- Prioritise and ration medicines
- Plan and coordinate delivery of services if needed
- Communicate information with NSW LHDs/SHNs about shortages and identified risks
- Provide advice to NSW LHDs/SHNs about what action can be taken to reduce identified risks
- Prepare information on clinical use and administration of the replacement product

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Communication

- Safety Alert Broadcast System
  - Safety Alert
  - Safety Notice
  - Safety Information
  - All are housed on intranet/internet site accessible by all NSW public health staff
- Memo and medication shortage communication sheet to NSW LHDs/SHNs
- Liaison with TGA and product sponsor

NSW Government, Health. Safety Alert Broadcast System (SABS). http://www.health.nsw.gov.au/sabs/pages/default.aspx. Accessed 31/01/2017.

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NSW GOVERNMENT Health

Safety Alert 002/16

Vancomycin Intravenous preparations – Disruption to supply

8 December 2016

Distributed to:
- Chief Executives
- Directors of Clinical Governance
- Director Regulation and Compliance Unit

Action required by:
- Chief Executives
- Directors of Clinical Governance

We recommend you also inform:
- Emergency Departments
- Intensive Care Units
- Infectious Diseases Physicians
- Cardiology
- Cardiothoracic surgery
- Orthopaedics
- Respiratory medicine
- Directors of Medical Services
- Directors of Nursing
- Directors of Pharmacy

Deadline for completion of action

12 December 2016

Expert Reference Group
Content reviewed by:
- Office of the Chief Health Officer
- Chief Pharmacist Unit
- Clinical Excellence Commission
- HealthShare
- AMS Expert Advisory Committee

Clinical Excellence Commission
Tel. 02 9269 5500
Fax. 02 9269 5599
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Cec-quality@health.nsw.gov.au
Internet Website:
http://www.health.nsw.gov.au/quality/sabs
Intranet Website
http://internal.health.nsw.gov.au/quality/sabs/

Review date

June 2017

Background

All three suppliers (Pfizer/Hospira, Alphapharm and Sandoz) in the Australian market have depleted stocks. A return to normal stock levels is expected in February 2017.

Vancomycin intravenous infusion is used for the treatment of potentially life threatening Gram-positive bacterial infections (suspected or known to be resistant to first-line antimicrobials) including bloodstream infections due to methicillin-resistant *Staphylococcus aureus* (MRSA).

Oral vancomycin is not absorbed systemically and is NOT a substitute for intravenous vancomycin.

The affected products are:

Presentation	AUST R
DBL Vancomycin (as hydrochloride) powder for injection 500 mg	62603
DBL Vancomycin (as hydrochloride) powder for injection 1 g	62595
Vancomycin Alphapharm (as hydrochloride) powder for injection 500 mg	153438
Vancomycin Alphapharm (as hydrochloride) powder for injection 1 g	153439
Vancomycin Sandoz (as hydrochloride) powder for injection 500 mg	100021
Vancomycin Sandoz (as hydrochloride) powder for injection 1 g	100011

Further Information

Pfizer has a limited quantity on hand of 500 mg powder for injection in 10 vial packs for restricted supply. They are in the process of investigating alternate supplies.

Actions required by Local Health Districts/Networks

1. Distribute this notice to all stakeholders and all clinical departments.
2. Assess the current status of vancomycin intravenous infusion preparations available in each facility, ensuring all locations of stock are identified. Provide feedback on stock levels to Clinical Excellence Commission cec-medicationsafety@health.nsw.gov.au by **COB Monday 12 December 2016.**
3. Remove and quarantine stock from clinical areas where vancomycin intravenous infusion preparations are not routinely used.
4. Use alternatives to intravenous vancomycin (e.g. intravenous teicoplanin) where possible, depending on the infection and patient factors. Clinicians that are unsure about the suitability of alternative antimicrobials should seek advice from antimicrobial stewardship teams and/or infectious diseases/clinical microbiology services.
5. The National Centre for Antimicrobial Stewardship provides some advice on suitable alternatives. Their factsheet is available at: https://www.ncas-australia.org/news-and-events
6. Reserve vancomycin injection for indications that cannot be treated by other available antimicrobials, based on the advice of infectious diseases/clinical microbiology services, according to antimicrobial stewardship processes.
7. Ensure a system is in place to document actions taken.

Safety Alerts require immediate attention and action

IV vancomycin:

- Released Safety Alert
- Gathered information on stock levels in NSW LHDs/SHNs
- Liaised with distributors about hospitals in urgent need of stock
- Updated Alert to include information on S19A approved substitute

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NSW GOVERNMENT Health

Safety Notice 012/16

Aciclovir intravenous infusion preparations – Disruption to supply (Revised on 13 December 2016)

13 December 2016

Distributed to:
- Chief Executives
- Directors of Clinical Governance
- Director Regulation and Compliance Unit

Action required by:
- Chief Executives
- Directors of Clinical Governance

We recommend you also inform:
- Emergency Departments
- Intensive Care Units
- Infectious Diseases Physicians
- Directors of Medical Services
- Directors of Nursing
- Directors of Pharmacy
- Neurology Departments

Expert Reference Group

Content reviewed by:
- Office of the Chief Health Officer
- Chief Pharmacist Unit
- Clinical Excellence Commission
- HealthShare
- AMS Expert Advisory Committee

Clinical Excellence Commission

Tel. 02 9269 5500
Fax. 02 9269 5599

Email:
cec-medicationsafety@health.nsw.gov.au

Internet Website:
http://www.health.nsw.gov.au/quality/sabs

Intranet Website
http://internal.health.nsw.gov.au/quality/sabs/

Review date
May 2017

Background

An out of stock notification has been received for aciclovir intravenous infusion preparations from the drug sponsor, Pfizer. This stock situation is due to unexpected maintenance work on the manufacturing line causing delay in production. There are current supply constraints with an expected out of stock period until **mid to late December 2016**.

Medsurge Healthcare P/L is able to supply an alternative product *Aciclovir 25 mg/mL Concentrate for solution for infusion* in both 250mg/10mL and 500mg/20mL vials on a temporary basis; this product is registered and marketed in the United Kingdom by Claris Lifesciences UK Limited. Although this product is not registered in Australia it can be supplied under an exemption granted by the Therapeutic Good Administration under section 19A of the Therapeutic Goods Act 1989.

Oral formulations of aciclovir are available.

Aciclovir intravenous infusion preparations are indicated for a number of manifestations of severe herpes simplex and varicella zoster infections.

The affected products are:

Presentation	AUST R
DBL™ Aciclovir Intravenous Infusion 250 mg/10 mL vials, 5 pack	56809
DBL™ Aciclovir Intravenous Infusion 500 mg/20 mL vials, 5 pack	56810
Aciclovir Intravenous Infusion 250 mg in 10 mL ampoules, 5 pack (Pfizer)	66116
Aciclovir Intravenous Infusion 500 mg in 20 mL ampoules, 5 pack (Pfizer)	66117

Further Information

Pfizer has a limited quantity on hand of aciclovir intravenous infusion for restricted supply on the basis of immediate patient use.

Therapeutic Goods Administration http://apps.tga.gov.au/prod/MSI/Search/Details/aciclovir

Suggested actions by Local Health Districts/Networks (until supply is reinstated):

1. Distribute this notice to all stakeholders and all clinical departments.
2. Assess the current status of aciclovir intravenous infusion preparations availability in each facility, ensuring all locations of stock are identified.
3. Remove and quarantine stock from clinical areas where aciclovir intravenous infusion preparations are not routinely used.
4. Consider restricting intravenous aciclovir to Infectious Disease approval only, using existing antimicrobial stewardship processes.
5. Limit treatment with aciclovir intravenous infusion preparations to those patients where treatment with an **intravenous** preparation is critical, such as patients with likely herpes simplex encephalitis, ophthalmic herpes zoster or immunocompromised patients with disseminated herpes zoster.
6. Ensure a system is in place to document actions taken.

Safety Notices require risk assessment at the local level

IV aciclovir:

- Released Safety Notice
- Updated Notice to include information on S19A approved substitute

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NSW Health

Medication Shortage Communication

Information for health professionals in NSW public health organisations

Piperacillin-tazobactam

Date of notice	29 May 2017 (revised 13 July 2017)
Status	Current
Details of the product(s) affected *Generic name, brand name(s), formulation(s) and strength(s)*	Generic name: Piperacillin-tazobactam Brand name: PiperTaz Tazopip Tazocin EF Formulations: Powder for infusion (intravenous) Strength: Piperacillin 4 g, tazobactam 500 mg
Reason for the shortage	Global manufacturing constraints
Date shortage notified or apparent	31 March 2017
Estimated resupply dates	20 October 2017 Supply is available, but constrained, in limited quantities to NSW public hospitals from Sandoz and Alphapharm.
Main therapeutic applications	Febrile neutropenia Serious bacterial infections caused by aerobic and/or anaerobic bacteria, especially if infection with *Pseudomonas aeruginosa* is suspected.
Alternative agents	Piperacillin-tazobactam is a very broad-spectrum penicillin antibiotic used for a wide range of infections. Suitable alternatives depend on the indication for antibiotic therapy; refer to *Therapeutic Guidelines (eTG complete)* for further guidance. For the treatment of febrile neutropenia, alternative agents include cefepime. Intravenous amoxycillin-clavulanic acid is active against Gram positive, Gram negative and anaerobic organisms, and is a suitable alternative to piperacillin-tazobactam for some indications where *Pseudomonas aeruginosa* cover is not required; speak to your infectious diseases, clinical microbiology or antimicrobial stewardship team/service. Antibiotic therapy with piperacillin-tazobactam should be reviewed once microbiology results are available, with a change to more narrow-spectrum therapy if appropriate. Existing stock of piperacillin-tazobactam should be reserved for infective conditions where piperacillin-tazobactam is the only available option. The National Centre for Antimicrobial Stewardship provides some advice on alternatives; refer to fact sheet available at: https://www.ncas-australia.org/education

NSW Health

Precautions associated with alternative products	Refer to the *Australian Medicines Handbook* (accessible from CIAP) for precautions associated with alternative antibiotic choices and further advice.
Anticipated effect of shortage on clinical practice	Judicious use of piperacillin-tazobactam. Action to address the shortage of piperacillin-tazobactam should be planned and implemented at a local level by the Antimicrobial Stewardship Committee and/or Drug and Therapeutics Committee. **Pharmacy departments from NSW public hospitals should ensure they have backorders in place for Sandoz and Alphapharm to receive an allocation.**
Associated regulatory/policy issues	PD2013_043 Medication Handling in NSW Public Health Facilities
Key contacts	Clinical Excellence Commission (Medication Safety): cec-medicationsafety@health.nsw.gov.au HealthShare NSW (Pharmaceutical Contracts): HSNSW-contract902@health.nsw.gov.au

Communication sheet to inform medium risk medication shortages - to be managed at the local level

IV piperacillin-tazobactam:

- Released memo and communication sheet

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NCAS Fact Sheets

- Provide general advice and possibilities for alternative therapy during times of short supply
- Ensure key messages of AMS are not lost in times of shortages
- Facilitate a consistent approach nationally to antibiotic shortages

https://www.ncas-australia.org/education

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Monitoring and feedback

- Regular dialogue maintained between product sponsor and MSAM team
  - Key changes or new information communicated to NSW LHDs/SHNs
- Surveillance of available datasets to detect any reported incidence of patient harm related to a medicines shortage
- Teleconferences to discuss shortages and provide updates to situation as needed

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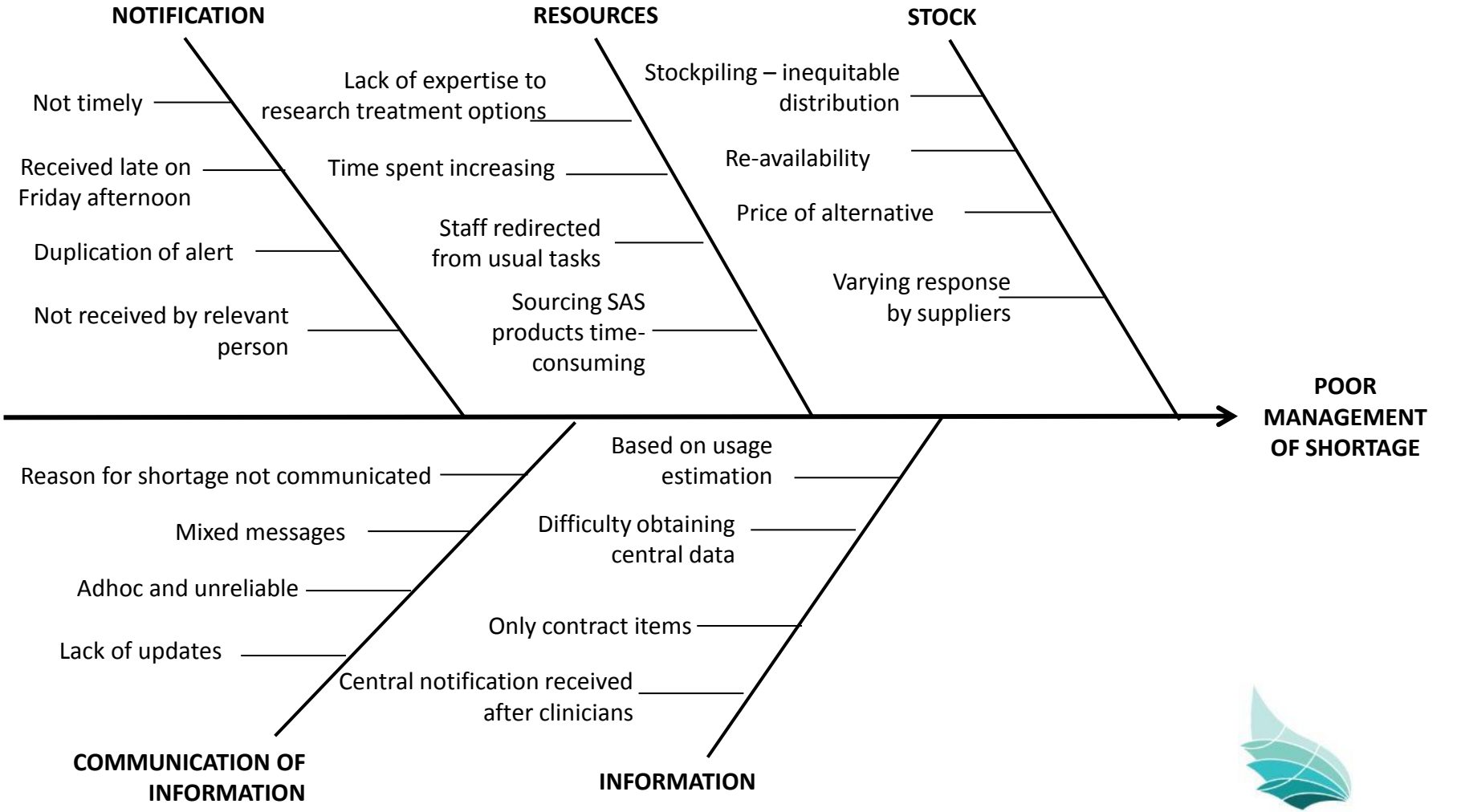
Factors affecting management of shortages



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Scope of problem in Australia

Daily Mail AUSTRALIA

Hospitals forced to stockpile and ration antibiotics as Australia faces an 'unbelievable' national shortage

By STEPHEN JOHNSON FOR DAILY MAIL AUSTRALIA
PUBLISHED: 16:47 +11:00, 11 December 2016 | **UPDATED:** 09:15 +11:00, 12 December 2016

Impact on hospital antimicrobial stewardship programs ??

The Sydney Morning Herald
NEWS SITE OF THE YEAR

DECEMBER 11 2016

'Patients will die if they don't fix this': Hospitals rationing, stockpiling first-line antibiotics amid drug shortage

Kate Aubusson

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Questions?

For further information:

CEC-MedicationSafety@health.nsw.gov.au

www.cec.health.nsw.gov.au

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