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RE: Shortage of Pfizer (Australia) DAUNORUBICIN (as hydrochloride) 20mg/10mL injection vial and alternative supply arrangement under Section 19A of the *Therapeutic Goods Act*.

Dear Healthcare Professional,

This notification is sent by LINK to inform your organisation that due to the shortage of Australian registered **Pfizer (Australia) DAUNORUBICIN (as hydrochloride) 20mg/10mL injection vial (AUST R 12723)**, LINK has arranged the supply of an alternative product **Daunorubicin (Zentiva) 20mg powder for injection vial** registered and marketed in *the United Kingdom.*

Daunorubicin (Zentiva) 20mg powder for injection vial is NOT registered in Australia and supply is authorised under an approval granted by the Therapeutic Goods Administration (TGA) under Section 19A of the *Therapeutic Goods Act, 1989* until **31 July 2022.**

Daunorubicin (Zentiva) 20mg powder for injection vials are indicated for:

Acute lymphocytic (lymphoblastic) leukaemia
Daunorubicin is usually reserved for use in cases shown to be resistant to other drugs. However, combined treatment with daunorubicin, vincristine and a steroid has been used in the early stages of this disease.

Acute myeloblastic leukaemia
Daunorubicin has been used in all stages, alone or in combination with other cytotoxic agents (e.g., cytarabine).

The s19A approved *UK* product is identical in active ingredient and strength to the Australian registered product. Please note the following information regarding differences between the two products.

	Pfizer (Australia) DAUNORUBICIN (as hydrochloride) 20mg/10mL injection vial (AUST R 12723)	**Daunorubicin (Zentiva) 20mg powder for injection vial**
Dose form	Solution for intravenous injection	lyophilised powder for intravenous administration
Excipients	Sodium chloride Water for injections	Mannitol
Storage	Store between 2°C to 8°C. Protect from light.	Store below 25°C and protect from light. After reconstitution Daunorubicin should be stored at 2 - 8°C, protected from light. After reconstitution Daunorubicin should be used within 24 hours.
Reconstitution and Preparation	It is recommended the injection be added to a free flowing IV infusion of 0.9% sodium chloride or 5% dextrose injection. The tubing should be connected to a butterfly needle, inserted preferably into a large vein. The dose and the size of	The contents of a vial should be reconstituted with 4ml of Water for Injection giving a concentration of 5 mg per ml. The calculated dose of Daunorubicin should be further diluted with normal saline to give a final concentration of 1 mg per ml.

	the vein will determine the rate of administration, which should not be less than 3-5 minutes. Erythematous streaking and facial flushing are indications of too rapid administration.	The solution should be injected over a 20-minute period into the tubing, or side arm, of a well-placed, rapidly flowing i.v. infusion of normal saline (to minimise extravasation and possible tissue necrosis). Alternatively, the Daunorubicin may be added to a minibag of sodium chloride injection 0.9% and this solution infused into the side arm of a rapidly flowing infusion of normal saline.
Dosage	The dosage of each individual injection may vary from 0.5 to 3 mg/kg, with the frequency of repetition according to the dose: • 0.5 to 1 mg/kg repeated at intervals of one or more days; • 2 mg/kg repeated at intervals of four or more days; • 2.5 or 3 mg/kg, if used, should only be given at seven to fourteen day intervals. Dosage must be adjusted to meet individual requirements of each patient, on the basis of clinical response and appearance or severity of toxicity. One injection has sometimes sufficed; commonly three to six injections have been necessary; occasionally up to 10 injections in one series have been used. When second or subsequent injections are to be given the doses and the time intervals depend on the effect of the previous doses and must be the subject of careful deliberation, examination of the peripheral blood and under some circumstances, of the marrow. The dosage of daunorubicin is usually based on the patient's body surface area (m2), but in paediatric patients younger than 2 years of age (or with a body surface area of less than 0.5 m2) it is suggested to calculate the dosage on the body weight (kg) rather than on body surface area.	**Adults**: 40 - 60 mg/m² on alternate days for a course of up to three injections for the induction of remissions. **Acute myelogenous leukaemia**: The recommended dose is 45 mg/m² **Acute lymphocytic leukaemia**: The recommended dose is 45 mg/m² **Paediatric population**: Daunorubicin dosage for children (over 2 years) is usually calculated based on the body surface area and adjusted to meet the individual requirements of each patient, on the basis of clinical response and the patients' haematological status. Courses may be repeated after 3 to 6 weeks. -Current specialised protocols and guidelines should be consulted for appropriate treatment regimen. For children over 2 years the maximal cumulative dose is 300 mg/m2. For children under 2 years of age (or below 0.5m2 body surface area), the maximum cumulative dose is 10mg/kg. **Elderly**: Daunorubicin should be used with care in patients with inadequate bone marrow reserves due to old age. A reduction of up to 50% in dosage is recommended. The number of injections required varies widely from patient to patient and must be determined in each case according to response and tolerance.

	For paediatric patients under 2 years of age (or below 0.5 m2 body surface area), the maximum cumulative dose is 10 mg/kg. For paediatric patients over 2 years, the maximal cumulative dose is 300 mg/m2. **Acute lymphocytic leukaemia** Doses of 1 mg/kg may be repeated according to tolerance and effect at one to four day intervals. **Acute myeloblastic leukaemia** Each dose should be about 2 mg/kg, more or less, according to effect, repeated at four to seven day intervals. Doses of over 2 mg/kg should be employed with caution at intervals of one week or longer.	Daunorubicin should be administered with caution when the neutrophil count is <1,500/mm3. Daunorubicin dose reduction should be considered in case of severe neutropenia. The dosage should be reduced in patients with impaired hepatic or renal function. A 25% reduction is recommended in patients with serum bilirubin concentrations of 20 -50 µmol/l or creatinine of 105 - 265 µmol/l. A 50% reduction is recommended in cases with serum bilirubin concentrations of above 50 µmol/l or creatinine of above 265 µmol/l. Daunorubicin is extremely irritating to tissues and may only be administered intravenously after dilution. Daunorubicin should be administered through a large vein and the infusion should be kept free flowing. When second or subsequent injections are given, the doses and time intervals depend on the effect of the previous doses and must be the subject of careful deliberation, examination of the peripheral blood and, under some circumstances, of the bone marrow.
Spills and disposal	If spills occur, restrict access to the affected area. Wear two pairs of gloves (latex rubber), a respirator mask, a protective gown and safety glasses. Limit the spread of the spill by covering with absorbent material such as absorbent towel or adsorbent granules. Spills may also be treated with 3M sulphuric acid and 0.3M potassium permanganate (2:1) or 5% sodium hypochlorite. Collect up the towel of absorbent/adsorbent material and other debris from spill and place in a leak proof plastic container labelled accordingly. Cytotoxic waste should be regarded as	Daunorubicin injection may be neutralised with sodium hypochlorite prior to disposal of unused drug or if a vial is accidently broken. The neutralised drug can be disposed of in the sink.

	hazardous or toxic and clearly labelled 'CYTOTOXIC WASTE FOR INCINERATION AT 1100°C'. Waste material should be incinerated for at least one second at 1100°C. Cleanse the remaining spill area with copious amounts of water.	

Daunorubicin (Zentiva) 20mg powder for injection vials are registered in ***the United Kingdom*** with the outer package and package insert in both English. The active ingredient, strength and dosage form included on the vial label are in English.

Please refer to the package insert for ***Daunorubicin (Zentiva) 20mg powder for injection vials*** for storage, reconstitution and preparation information. For dosing and prescribing information, please refer to the Australian Product Information (PI) for **Pfizer (Australia) DAUNORUBICIN (as hydrochloride) 20mg/10mL injection vial (AUST R 12723)** (available at https://www.ebs.tga.gov.au) **.**

Adverse Event Reporting

Reporting any suspected adverse event is important for the continued monitoring of the safety of all medicines. Any adverse events which are experienced with ***Daunorubicin (Zentiva) 20mg powder for injection vial*** should be reported by healthcare professionals and patients to Link Healthcare Medical Information. This information can also be reported to the TGA at https://www.tga.gov.au/reporting-problems.

Link Healthcare Medical Information can be contacted by phone on 1800 181 060 or via email at medinfo@linkhealthcare.com.au.

Link Healthcare Customer Service contact details

Link Healthcare Customer Service can be contacted via phone on 1800 181 060 or via email at customerservice@linkhealthcare.com.au.

Please contact Link Healthcare Customer Service for further information.

We would appreciate if you could distribute this information to those in your organisation who would be affected by the shortage of the Australian registered **Pfizer (Australia) DAUNORUBICIN (as hydrochloride) 20mg/10mL injection vial (AUST R 12723).**

Yours sincerely,

C Griffin

Charlotte Griffin
Medicine Access Associate