

**OOS DAUNORUBICIN WITH CYTARABINE,
Powder for I.V. infusion containing daunorubicin
44 mg and cytarabine 100 mg,
Vyxeos[®],
Jazz Pharmaceuticals ANZ Pty Ltd.**

1 Purpose of submission

- 1.1 To seek the PBAC's advice on the interim listing of liposomal daunorubicin and cytarabine (Vyxeos[®]) on the Section 100 Highly Specialised Drugs (HSD) Program, while system and administrative issues relating to a Section 100 Efficient Funding of Chemotherapy (EFC) listing are being worked through.
- 1.2 The PBAC was requested to note that under Section 100 EFC, patients are not required to pay a co-payment for the supply of a repeat prescription but would be required to do so under Section 100 HSD.

2 Background

- 2.1 In November 2023, the PBAC recommended the listing of liposomal daunorubicin and cytarabine for the treatment of patients with therapy-related acute myeloid leukaemia (t-AML) or acute myeloid leukaemia with myelodysplasia-related changes (AML-MRC), on the basis that it should be available only under special arrangements under Section 100 EFC.
- 2.2 Liposomal daunorubicin and cytarabine is a combination chemotherapy product, has a different dosage than daunorubicin injection and cytarabine injection and it must not be interchanged with other daunorubicin and/or cytarabine-containing products.
- 2.3 Dosing for liposomal daunorubicin and cytarabine is based on the patient's body surface area (BSA) according to the TGA approved Product Information dosing schedule:

Table 1: Dose and schedule for liposomal daunorubicin and cytarabine in patients with newly diagnosed t-AML or AML-MRC

Therapy	Dose and dose schedule
First induction	daunorubicin 44 mg/m ² and cytarabine 100 mg/m ² on days 1, 3, and 5
Second induction	daunorubicin 44 mg/m ² and cytarabine 100 mg/m ² on days 1 and 3
Consolidation	daunorubicin 29 mg/m ² and cytarabine 65 mg/m ² on days 1 and 3

Source: Vyxeos Product Information page 2

Abbreviations: t-AML = therapy-related acute myeloid leukaemia, AML-MRC = acute myeloid leukaemia with myelodysplasia-related changes

- 2.4 At present, the EFC pricing algorithm is not designed to accommodate combination products. Further, the addition of a Section 100 EFC combination product presents system challenges for Services Australia, prescribing software vendors and dispensing

Public Summary Document – April 2024 PBAC Out-of-Session Consideration

software vendors around correct dose calculation and payment as per the EFC algorithm as these systems are also not currently equipped to manage combination dose EFC medicines. It is expected that significant changes to software, the EFC calculation algorithm and Services Australia systems would be required, potentially delaying implementation of a PBS listing.

- 2.5 Following the PBAC recommendation, the Department considered alternative options to progress a listing ahead of required changes being made to relevant legislative instruments and information technology (IT) systems. One of these options included an interim listing on the Section 100 HSD Program.
- 2.6 Other products for intravenous infusion are available under Section 100 HSD arrangements (e.g. rituximab, doxorubicin – pegylated liposomal). Further, relatlimab and nivolumab, a fixed dose combination therapy, was originally recommended for listing on the Section 100 EFC Program and moved as an interim listing on the Section 100 HSD Program due to similar challenges (paragraphs 7.1 and 12.1, relatlimab and nivolumab, Public Summary Document, March 2023 PBAC Meeting with July 2023 Addendum). However, unlike relatlimab and nivolumab, liposomal daunorubicin and cytarabine does not have fixed dosing and is a cytotoxic medicine.
- 2.7 The proposed Section 100 HSD listing includes an additional prescribing instruction to ensure prescribers and Services Australia are able to determine and approve an appropriate maximum quantity of vials for patients based on their BSA. This would allow the listing to progress on the HSD in the absence of an EFC algorithm that is able to accommodate two maximum amounts.

3 Requested Section 100 HSD listing

3.1 Details of the request to list Vyxeos is outlined in Table 2 below.

MEDICINAL PRODUCT Form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
<i>LIPOSOMAL DAUNORUBICIN with CYTARABINE</i>					
<i>liposomal daunorubicin hydrochloride 44 mg plus cytarabine 100 mg injection, 1 vial</i>	<i>NEW (Public) NEW (Private)</i>	3	3	4	Vyxeos
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	Category / Program: Section 100 – <i>Highly Specialised Drugs Program (Public and Private Hospitals)</i>				
	Prescriber type: Medical Practitioners				
	Restriction type: Authority Required (telephone/online PBS Authorities system)				
	Indication: Acute myeloid leukaemia				
	Treatment phase: Induction				
	Clinical criteria:				
	Patient must not have received prior chemotherapy as induction therapy for this condition				
	AND				
	Clinical criteria:				

Public Summary Document – April 2024 PBAC Out-of-Session Consideration

	The condition must be either (i) newly diagnosed therapy-related acute myeloid leukaemia (AML), (ii) newly diagnosed AML with myelodysplasia-related changes (MRC) (prior myelodysplastic syndromes (MDS) or MDS-related cytogenetic or molecular abnormality),
	AND
	Clinical criteria:
	The condition must not be either (i) internal tandem duplication (ITD), or (ii) tyrosine kinase domain (TKD) FMS tyrosine kinase 3 (FLT3), mutation positive
	AND
	Clinical criteria:
	Patient must not have favourable cytogenetic risk AML
	AND
	Clinical criteria:
	Patient must have a World Health Organization (WHO) performance status score of 2 or less.
	Treatment criteria:
	The treatment must not exceed two cycles of induction therapy under this restriction.
	Prescribing Instructions: This product is not PBS-subsidised if it is administered to an in-patient in a public hospital setting.
	Prescribing Instructions: The prescriber must confirm whether the patient has newly diagnosed therapy-related AML or AML-MRC. The test result and date of testing must be provided at the time of application and documented in the patient's file.
	<i>The TGA approved Product Information recommended dosing schedule is as follows:</i> (i) First Induction: daunorubicin 44mg/m ² and cytarabine 100mg/m ² on days 1, 3 and 5 (ii) Second Induction: daunorubicin 44mg/m ² and cytarabine 100mg/m ² on days 1 and 3 <i>With each authority application, state the body surface area (m²) of the patient.</i> <i>Based on (i) to (ii), prescribe up to:</i> 1 vial where the body surface area is up to and including 1m ² ; 2 vials where the body surface area is above 1m ² or up to and including 2m ² 3 vials where the body surface area is above 2m ² or up to and including 3m ²
	Caution: Liposomal daunorubicin and cytarabine (Vyxeos) must not be substituted or interchanged with other daunorubicin and/or cytarabine containing products. Due to substantial differences in the pharmacokinetic parameters, the dose and schedule recommendations for Vyxeos are different from other medications that contain daunorubicin and/or cytarabine in other forms.
	Administrative advice: No increase in the maximum number of repeats may be authorised.
	Administrative advice: Special Pricing Arrangements apply.
	Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

MEDICINAL PRODUCT Form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
LIPOSOMAL DAUNORUBICIN with CYTARABINE					
<i>liposomal daunorubicin hydrochloride 44 mg plus cytarabine 100 mg injection, 1 vial</i>	<i>NEW (Public) NEW (Private)</i>	2	2	3	Vyxeos
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID	Category / Program: Section 100 – Highly Specialised Drugs Program (Public and Private Hospitals)				

Public Summary Document – April 2024 PBAC Out-of-Session Consideration

(for internal Dept. use)	Prescriber type: Medical Practitioners
	Restriction type: Authority Required (telephone/online PBS Authorities system)
	Indication: Acute myeloid leukaemia
	Treatment phase: Consolidation
	Clinical criteria:
	The treatment must be for consolidation treatment following induction treatment with this product.
	AND
	Clinical criteria:
	The condition must be either (i) newly diagnosed therapy-related acute myeloid leukaemia (AML), (ii) newly diagnosed AML with myelodysplasia-related changes (MRC) (prior myelodysplastic syndromes (MDS) or MDS-related cytogenetic or molecular abnormality),
	Treatment criteria:
	The treatment must not exceed two cycles of consolidation therapy under this restriction.
	Prescribing Instructions: This product is not PBS-subsidised if it is administered to an in-patient in a public hospital setting.
	<i>The TGA approved Product Information recommended dosing schedule for consolidation is daunorubicin 29mg/m² and cytarabine 65mg/m² on days 1 and 3</i>
	<i>With each authority application, state the body surface area (m²) of the patient.</i>
	<i>Based on this prescribe up to:</i>
	<i>1 vial where the body surface area is between 1m² to 1.53m²</i>
	<i>2 vials where the body surface area is above 1.53m² or up to and including 3.07m²</i>
	Caution: Liposomal daunorubicin and cytarabine (Vyxeos) must not be substituted or interchanged with other daunorubicin and/or cytarabine containing products. Due to substantial differences in the pharmacokinetic parameters, the dose and schedule recommendations for Vyxeos are different from other medications that contain daunorubicin and/or cytarabine in other forms.
	Administrative advice: No increase in the maximum number of repeats may be authorised.
	Administrative advice: Special Pricing Arrangements apply.
	Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

4 PBAC outcome

- 4.1 The PBAC recommended liposomal daunorubicin and cytarabine (Vyxeos) be listed on the Section 100 HSD Program as an interim listing, while system and administrative issues relating to a Section 100 EFC listing are being resolved.
- 4.2 The PBAC noted that, under Section 100 EFC, patients are not required to pay a co-payment for the supply of a repeat prescription but would be required to do so under Section 100 HSD. The PBAC acknowledged the additional financial burden this may place on patients, however the availability of liposomal daunorubicin and cytarabine on Section 100 HSD provides for subsidised access that would not be available if a Section 100 HSD listing was not considered.

4.3 The PBAC considered the additional prescribing instructions for liposomal daunorubicin and cytarabine listings are appropriate.

Outcome:

Recommended

5 Recommended listing

5.1 Add new item:

MEDICINAL PRODUCT Form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
<i>LIPOSOMAL DAUNORUBICIN with CYTARABINE</i>					
<i>liposomal daunorubicin hydrochloride 44 mg plus cytarabine 100 mg injection, 1 vial</i>	<i>NEW (Public) NEW (Private)</i>	3	3	4	Vyxeos
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	Category / Program: Section 100 – <i>Highly Specialised Drugs Program (Public and Private Hospitals)</i>				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Indication: Acute myeloid leukaemia				
	Treatment phase: Induction				
	Clinical criteria:				
	Patient must not have received prior chemotherapy as induction therapy for this condition				
	AND				
	Clinical criteria:				
	The condition must be either (i) newly diagnosed therapy-related acute myeloid leukaemia (AML), (ii) newly diagnosed AML with myelodysplasia-related changes (MRC) (prior myelodysplastic syndromes (MDS) or MDS-related cytogenetic or molecular abnormality),				
	AND				
	Clinical criteria:				
	The condition must not be either (i) internal tandem duplication (ITD), or (ii) tyrosine kinase domain (TKD) FMS tyrosine kinase 3 (FLT3), mutation positive				
	AND				
	Clinical criteria:				
	Patient must not have favourable cytogenetic risk AML				
	AND				
	Clinical criteria:				
	Patient must have a World Health Organization (WHO) performance status score of 2 or less.				
	Treatment criteria:				
	The treatment must not exceed two cycles of induction therapy under this restriction.				
	Prescribing Instructions: This product is not PBS-subsidised if it is administered to an in-patient in a public hospital setting.				
	Prescribing Instructions: The prescriber must confirm whether the patient has newly diagnosed therapy-related AML or AML-MRC. The test result and date of testing must be provided at the time of application and documented in the patient's file.				

Public Summary Document – April 2024 PBAC Out-of-Session Consideration

<p>The TGA approved Product Information recommended dosing schedule is as follows:</p> <p>(i) First Induction: daunorubicin 44mg/m² and cytarabine 100mg/m² on days 1, 3 and 5</p> <p>(ii) Second Induction: daunorubicin 44mg/m² and cytarabine 100mg/m² on days 1 and 3</p> <p>With each authority application, state the body surface area (m²) of the patient.</p> <p>Based on (i) to (ii), prescribe up to:</p> <p>1 vial where the body surface area is up to and including 1m²;</p> <p>2 vials where the body surface area is above 1m² or up to and including 2m²</p> <p>3 vials where the body surface area is above 2m² or up to and including 3m²</p>
<p>Caution: Liposomal daunorubicin and cytarabine (Vyxeos) must not be substituted or interchanged with other daunorubicin and/or cytarabine containing products. Due to substantial differences in the pharmacokinetic parameters, the dose and schedule recommendations for Vyxeos are different from other medications that contain daunorubicin and/or cytarabine in other forms.</p>
<p>Administrative advice: No increase in the maximum number of repeats may be authorised.</p>
<p>Administrative advice: Special Pricing Arrangements apply.</p>
<p>Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).</p>

MEDICINAL PRODUCT Form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
<i>LIPOSOMAL DAUNORUBICIN with CYTARABINE</i>					
<i>liposomal daunorubicin hydrochloride 44 mg plus cytarabine 100 mg injection, 1 vial</i>	<i>NEW (Public) NEW (Private)</i>	2	2	3	Vyxeos
Restriction Summary [new] / Treatment of Concept: [new]					
Concept ID (for internal Dept. use)	Category / Program: Section 100 – <i>Highly Specialised Drugs Program (Public and Private Hospitals)</i>				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Indication: Acute myeloid leukaemia				
	Treatment phase: Consolidation				
	Clinical criteria:				
	The treatment must be for consolidation treatment following induction treatment with this product.				
	AND				
	Clinical criteria:				
	The condition must be either (i) newly diagnosed therapy-related acute myeloid leukaemia (AML), (ii) newly diagnosed AML with myelodysplasia-related changes (MRC) (prior myelodysplastic syndromes (MDS) or MDS-related cytogenetic or molecular abnormality),				
	Treatment criteria:				
	The treatment must not exceed two cycles of consolidation therapy under this restriction.				
	Prescribing Instructions: This product is not PBS-subsidised if it is administered to an in-patient in a public hospital setting.				
	<p>The TGA approved Product Information recommended dosing schedule for consolidation is daunorubicin 29mg/m² and cytarabine 65mg/m² on days 1 and 3</p> <p>With each authority application, state the body surface area (m²) of the patient.</p>				

Public Summary Document – April 2024 PBAC Out-of-Session Consideration

	Based on this prescribe up to: 1 vial where the body surface area is between 1m ² to 1.53m ² 2 vials where the body surface area is above 1.53m ² or up to and including 3.07m ²
	Caution: Liposomal daunorubicin and cytarabine (Vyxeos) must not be substituted or interchanged with other daunorubicin and/or cytarabine containing products. Due to substantial differences in the pharmacokinetic parameters, the dose and schedule recommendations for Vyxeos are different from other medications that contain daunorubicin and/or cytarabine in other forms.
	Administrative advice: No increase in the maximum number of repeats may be authorised.
	Administrative advice: Special Pricing Arrangements apply.
	Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

The sponsor had no comment.