

**5.14 DEFERASIROX,  
Tablet 125 mg, 250 mg, 500 mg dispersible,  
Deferasirox Juno<sup>®</sup>,  
Juno Pharmaceuticals Pty Ltd**

**1 Purpose of Application**

- 1.1 The minor submission requested the Section 100 Highly Specialised Drugs (S100 HSD) Program listing of deferasirox 125 mg, 250 mg and 500 mg dispersible tablets (Deferasirox Juno<sup>®</sup>, DFXJ from herein) for patients with chronic iron overload due to disorders of haemopoiesis.
- 1.2 Listing was requested on a cost-minimisation basis to deferasirox 90 mg, 180 mg and 360 mg film coated tablets (Jadenu<sup>®</sup>). Listing was requested under the same conditions as Jadenu.
- 1.3 DFXJ was developed as a generic formulation of the previously PBS-listed Exjade<sup>®</sup>, which was delisted on 1 May 2019 following the listing of Jadenu. Exjade and Jadenu had the same sponsor (Novartis).

**2 Background**

***Registration status***

- 2.1 DFXJ was first TGA registered on 7 November 2019.

***Previous PBAC consideration***

- 2.2 A summary of previous PBAC considerations for deferasirox is shown in Table 1.

**Table 1: Previous PBAC considerations for deferasirox**

Product	Purpose of application	PBAC meeting date	Outcome	Detail
Deferasirox 125 mg, 250 mg and 500 mg dispersible tablets (Exjade)	To seek listing on the S100 HSD program for chronic iron overload associated with the treatment of disorders of erythropoiesis.	July 2006	Recommended	The PBAC recommended listing on a cost effectiveness basis versus the comparator, desferrioxamine, noting that the incremental cost-effectiveness ratio was somewhat uncertain and is likely to be high.
Deferasirox 125 mg, 250 mg and 500 mg dispersible tablets (Exjade)	To seek listing on the S100 HSD program for the treatment of iron overload associated with transfusion dependent malignant disorder of erythropoiesis and non-transfusion dependent thalassaemia.	July 2015	Rejected	The PBAC rejected the submission to retain the current PBS restriction for DFX for patients with “chronic iron overload in patients with disorders of erythropoiesis” as the broad restriction enabled major use outside populations where cost-effectiveness had been demonstrated, in particular myelodysplasia
Deferasirox 90 mg, 180 mg, 360 mg film coated tablets (Jadenu)	To seek listing on the S100 HSD program for patients with chronic iron overload due to disorders of haemopoiesis.	July 2018	Recommended	The PBAC recommended the listing on a cost minimisation basis with deferasirox dispersible tablets. The PBAC’s recommendation for listing was based on, among other matters, its assessment that deferasirox film coated tablets, while not strictly bioequivalent, were biocomparable to deferasirox dispersible tablets.

### 3 Requested listing

3.1 The submission requested that DFXJ be listed under the same restriction criteria as Jadenu.

*For more detail on PBAC’s view, see section 6 PBAC outcome.*

### 4 Comparator

4.1 The minor submission nominated Jadenu as the main comparator. The PBAC considered that this was appropriate.

4.2 In its consideration of Jadenu in July 2018, the PBAC considered that Jadenu and Exjade, while not strictly bioequivalent, were biocomparable (paragraph 6.1, deferasirox Public summary document (PSD), July 2018 PBAC meeting).

- 4.3 Based on the results of the ECLIPSE trial provided with the July 2018 submission for Jadenu, the PBAC considered that Jadenu was non-inferior to Exjade, and therefore a cost-minimisation approach was appropriate (paragraph 6.6, deferasirox PSD, July 2018).
- 4.4 The PBAC advised that the equi-effective doses of deferasirox were (paragraph 6.7, deferasirox PSD, July 2018):
- 360 mg film coated tablet = 500 mg dispersible tablet
  - 180 mg film coated tablet = 250 mg dispersible tablet
  - 90 mg film coated tablet = 125 mg dispersible tablet

*For more detail on PBAC's view, see section 6 PBAC outcome.*

## **5 Consideration of the evidence**

### ***Sponsor hearing***

- 5.1 There was no hearing for this item as it was a minor submission.

### ***Consumer comments***

- 5.2 The PBAC noted that no consumer comments were received for this item.

### ***Clinical trials***

- 5.3 There were no clinical trials presented with the minor submission.
- 5.4 The basis of the minor submission's request was that DFXJ was developed as a generic formulation of Exjade, which was considered by the PBAC to be biocomparable and non-inferior to Jadenu (paragraph 6.3 and 6.6, deferasirox PSD, July 2018 PBAC meeting).
- 5.5 The minor submission stated that this was confirmed by an open label, balanced, randomized, two-treatment, two-period, two-sequence, two-way crossover oral bioequivalence study that was conducted with DFXJ 500 mg using Exjade 500 mg as the reference product. The minor submission stated that the study was open label in nature because blood concentration levels cannot be influenced by knowledge of the identity of the treatment, and that use of a crossover design was appropriate since it enables comparison of treatments within the same study participant using intra-subject variability thus improving the precision of treatment comparisons.
- 5.6 The TGA clinical evaluation report concluded that, on the basis of the results of this study, DFXJ 500 mg and Exjade 500 mg were bioequivalent.

### ***Clinical claim***

- 5.7 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of DFXJ compared with Jadenu.

5.8 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonably supported by the data.

**Economic analysis**

5.9 As a minor submission, the economic analysis has not been independently evaluated.

5.10 The minor submission proposed the same price per tablet between the equi-effective doses of Jadenu and DFXJ (see paragraph 4.4). The proposed pricing is shown in Table 2.

**Table 2: Pricing of current Jadenu presentations and proposed pricing of DFXJ using published prices**

Medicine	Pack size	AEMP	Price per tablet
Jadenu 90 mg film coated tablet	30	\$213.98	\$7.13
DFXJ 125 mg dispersible tablet	28	\$199.71	\$7.13
Jadenu 180 mg film coated tablet	30	\$427.94	\$14.26
DFXJ 250 mg dispersible tablet	28	\$399.41	\$14.26
Jadenu 360 mg film coated tablet	30	\$855.89	\$28.53
DFXJ 500 mg dispersible tablet	28	\$798.83	\$28.53

Source: Submission Table 3.1 and 3.2

**Drug cost/patient/year: \$ [REDACTED]**

5.11 The minor submission stated that the drug cost per patient per year could not be estimated as the clinical management of iron overload and iron chelation varies from patient to patient and is entirely dependent on their serum ferritin levels rather than on a set course or treatment duration.

5.12 Based on the 2021 script estimates (see Table 3), the Secretariat estimates that the cost per script would be net cost (\$ [REDACTED] / total scripts (500 to < 5,000) = \$ [REDACTED], and assuming 13.04 scripts per year, this would equate to an annual costs per patient of (\$ [REDACTED] x 13.04) = \$ [REDACTED].

**Estimated PBS usage & financial implications**

5.13 The minor submission used a market share approach to estimate the financial impact of DFXJ.

5.14 The submission used historical PBS data from 2013-2019 for Exjade and data from 1 December 2018 for Jadenu to forecast the PBS utilisation from 2020-2026 for DFXJ over Jadenu.

5.15 The minor submission noted that a special pricing arrangement (SPA) is in place for Jadenu, and estimated a net cost to the PBS of \$0 to <10 million in Year 6 of listing using published prices, with a total net cost to the PBS of \$0 to <\$10 million over the first 6 years of listing (Table 3).

**Table 3: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated financial implications of DFXJ</b>						
Number of scripts dispensed	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>
Cost to PBS/RPBS	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>
Co-payments	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>
Cost to PBS/RPBS less co-payments	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>
<b>Estimated financial implications for Jadenu</b>						
Forecasted change to PBS/RPBS Jadenu scripts	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>
Savings to PBS/RPBS	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>
Co-payments	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>
Savings to PBS/RPBS less co-payments	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>	-\$█ <sup>3</sup>
<b>Net financial implications</b>						
Net impact to scripts	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>
Net cost/savings to PBS/RPBS	-\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>	\$█ <sup>3</sup>

Source: Table 4.6, 4.7, 4.8, 4.9, 4.10 of the submission.

The redacted values correspond to the following ranges:

<sup>1</sup>500 to <5,000

<sup>2</sup><500

<sup>3</sup>\$0 to <\$10 million

- 5.16 The costs to the PBS result from pack size difference between DFXJ (28 tablets) and Jadenu (30 tablets) which results in a slight difference in script volumes and co-payments.
- 5.17 The submission stated that the net cost to the PBS has been slightly overstated in later years because co-payment amounts had been assumed to remain constant throughout the forward estimates period.
- 5.18 As a minor submission, the financial estimates have not been independently evaluated.
- 5.19 The minor submission stated that upon receiving a positive recommendation from the PBAC, the sponsor may propose an increase in the rebates or consider requesting the removal of the SPA. The sponsor did not specify whether the potential proposed increase in rebates referred to an SPA or RSA rebate.

### **Quality use of medicine**

- 5.20 The minor submission claimed that listing deferasirox dispersible tablets offers an alternative administration method for patients who have swallowing difficulties and/or are unable/prefer not to crush/sprinkle the film coated deferasirox tablets on soft foods.

*For more detail on PBAC's view, see section 6 PBAC outcome.*

## **6 PBAC Outcome**

- 6.1 The PBAC recommended the listing of DFXJ on the S100 HSD Program for patients with chronic iron overload due to disorders of haemopoiesis on a cost-minimisation basis to Jadenu.
- 6.2 The PBAC reaffirmed that DFXJ was biocomparable to Jadenu and that the equi-effective doses were:
- 360 mg film coated tablet = 500 mg dispersible tablet
  - 180 mg film coated tablet = 250 mg dispersible tablet
  - 90 mg film coated tablet = 125 mg dispersible tablet
- 6.3 The PBAC noted that costs to the PBS would be incurred because DFXJ has 28 tablets per pack compared to Jadenu which has 30 tablets, and therefore prescription numbers for DFXJ would be higher. The PBAC considered that, given this recommendation is on a cost-minimisation basis, the listing should not result in any additional cost to government, as it is expected to share the market with Jadenu.
- 6.4 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because DFXJ is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Jadenu, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.
- 6.5 The PBAC advised that deferasirox is not suitable for prescribing by nurse practitioners.
- 6.6 The PBAC advised that the Early Supply Rule should apply as it currently applies to Jadenu.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 7 Recommended listing

Add new item:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DEFERASIROX deferasirox 125 mg dispersible tablet, 28	NEW	6	168	2	Deferasirox Juno
deferasirox 250 mg dispersible tablet, 28	NEW	6	168	2	Deferasirox Juno
deferasirox 500 mg dispersible tablet, 28	NEW	6	168	2	Deferasirox Juno

**Initial treatment in patients with transfusion dependent malignant disorders of haemopoiesis and a median life expectancy exceeding five years**

### Restriction Summary 8239 / Treatment of Concept: 7385

<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
<b>Administrative Advice:</b> Special Pricing Arrangements apply
<b>Indication:</b> Chronic iron overload
<b>Treatment Phase:</b> Initial treatment
<b>Clinical criteria:</b>
Patient must be red blood cell transfusion dependent
<b>AND</b>
Patient must have a serum ferritin level of greater than 1000 microgram/L
<b>AND</b>
Patient must have a malignant disorder of haemopoiesis
<b>AND</b>
Patient must have a median life expectancy exceeding five years
<b>Administrative Advice:</b> Special Pricing Arrangements apply
A patient's median life expectancy is determined by the severity of their underlying disease.
Patients with underlying myelodysplastic syndrome are considered to have a median life expectancy exceeding five years if they are classified as: - low risk according to the International Prognostic Scoring System (IPSS); or - very low and low risk according to the Revised International Prognostic Scoring System (IPSS-R); or - very low and low risk according to the WHO classification based Prognostic Scoring System (WPSS).
Patients with underlying myelofibrosis have a median life expectancy exceeding five years if they are classified as: - low or intermediate risk according to the International Prognostic Scoring System (IPSS); or - low or intermediate-1 risk according to Dynamic International Prognostic Scoring System (DIPSS).

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**Continuing treatment in patients with transfusion dependent malignant disorders of haemopoiesis and a median life expectancy exceeding five years**

**Restriction Summary 9258 / Treatment of Concept: 9258**

<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required – Streamlined
<b>Administrative Advice:</b> Special Pricing Arrangements apply
<b>Indication:</b> Chronic iron overload
<b>Treatment Phase:</b> Continuing treatment
<b>Clinical criteria:</b>
Patient must be red blood cell transfusion dependent
<b>AND</b>
Patient must have a malignant disorder of haemopoiesis
<b>AND</b>
Patient must have previously received PBS-subsidised treatment with deferasirox for this condition
<b>Administrative Advice:</b> Special Pricing Arrangements apply
Interruption of treatment should be considered if serum ferritin levels fall consistently below 500 microgram/mL.

**Initial treatment for patients with transfusion dependent non-malignant disorders of erythropoiesis**

**Restriction Summary 8235 / Treatment of Concept: 7375**

<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
<b>Administrative Advice:</b> Special Pricing Arrangements apply
<b>Indication:</b> Chronic iron overload
<b>Treatment Phase:</b> Initial treatment
<b>Clinical criteria:</b>
Patient must be transfusion dependent
<b>AND</b>
Patient must not have a malignant disorder of erythropoiesis
<b>Administrative Advice:</b> Special Pricing Arrangements apply

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**Continuing treatment for patients with transfusion dependent non-malignant disorders of erythropoiesis**

**Restriction Summary 9302 / Treatment of Concept: 9302**

	<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required – Streamlined
	<b>Administrative Advice:</b> Special Pricing Arrangements apply
	<b>Indication:</b> Chronic iron overload
	<b>Treatment Phase:</b> Continuing treatment
	<b>Clinical criteria:</b>
	Patient must be transfusion dependent
	<b>AND</b>
	Patient must not have a malignant disorder of erythropoiesis
	<b>AND</b>
	Patient must have previously received PBS-subsidised treatment with deferasirox for this condition
	<b>Administrative Advice:</b> Special Pricing Arrangements apply

**Initial treatment for patients with non-transfusion dependent thalassaemia**

**Restriction Summary 8236 / Treatment of Concept: 7374**

	<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
	<b>Administrative Advice:</b> Special Pricing Arrangements apply
	<b>Indication:</b> Chronic iron overload
	<b>Treatment Phase:</b> Initial treatment
	<b>Clinical criteria:</b>
	Patient must not be transfusion dependent
	<b>AND</b>
	The condition must be thalassaemia
	<b>Administrative Advice:</b> Special Pricing Arrangements apply

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**Continuing treatment for patients with non-transfusion dependent thalassaemia**

**Restriction Summary 9222 / Treatment of Concept: 9222**

<b>Category / Program:</b> Section 100 – Highly Specialised Drugs Program
<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
<b>Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required):</b> <input checked="" type="checkbox"/> Authority Required - Streamlined
<b>Administrative Advice:</b> Special Pricing Arrangements apply
<b>Indication:</b> Chronic iron overload
<b>Treatment Phase:</b> Continuing treatment
<b>Clinical criteria:</b> Patient must not be transfusion dependent
<b>AND</b> The condition must be thalassaemia
<b>AND</b> Patient must have previously received PBS-subsidised treatment with deferasirox for this condition
<b>Administrative Advice:</b> Special Pricing Arrangements apply

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

## **8 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.

## **9 Sponsor's Comment**

The sponsor had no comment.