

6.10 IRON SUCROSE

**iron (as sucrose) 100 mg/5 mL injection, 5 x 5 mL ampoules;
Venofer[®]; Aspen Pharmacare Australia Pty Ltd.**

1 Purpose of Application

- 1.1 The minor submission sought to amend the current listing for iron sucrose to be consistent to that of iron polymaltose by:
- 1) Requesting the same restriction as iron polymaltose (i.e. make the existing restriction less restrictive); and
 - 2) Offering a price reduction to achieve price parity with iron polymaltose.

2 Background

- 2.1 Iron sucrose was TGA registered on 19 May 2004 for the treatment of iron deficiency anaemia in patients undergoing chronic haemodialysis and who are receiving supplemental erythropoietin therapy.
- 2.2 In November 2004, the PBAC recommended listing iron sucrose as an Authority required benefit on the basis of acceptable cost effectiveness in patients who have failed prior IV iron polymaltose therapy due to hypersensitivity reactions.
- 2.3 In November 2007, the PBAC rejected a minor submission seeking derestriction of the current Section 85 listing to an 'unrestricted benefit' and, addition of a Section 100 listing for the treatment of iron deficiency anaemia in patients undergoing chronic haemodialysis and who are receiving supplemental erythropoietin therapy. The PBAC considered that insufficient data had been provided to recommend first-line listing of this product and that a major submission with a full cost-effectiveness analysis demonstrating superior efficacy and or safety compared with iron polymaltose would be required to do so. Further, given the restricted TGA indication for this product, the PBAC did not consider an unrestricted listing appropriate, but indicated that it would be prepared to consider a first-line restricted benefit listing if a major submission is provided. A Section 100 listing was not recommended as iron sucrose was not considered to be a 'highly specialised' drug.
- 2.4 At the April 2013 Special PBAC meeting, the PBAC considered and agreed to a request to increase the number of repeats available on the currently listed injectable iron preparations, iron polymaltose and iron sucrose, to five for patients undergoing haemodialysis. Following sponsor comment, at the July 2013 PBAC meeting, the PBAC recommended that the maximum quantity for iron sucrose's haemodialysis listing be amended back to 1.

3 Requested listing

- 3.1 The submission sought the following changes to the existing restriction and price as shown by italics and strikethrough:

Add new unrestricted benefit listing:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
IRON SUCROSE IRON (AS SUCROSE) 100 MG/5 ML INJECTION, 5 X 5 ML AMPOULES	1	0	Venofer	AS

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction level:	Unrestricted

Amend existing listing to be identical to iron polymaltose:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
IRON SUCROSE IRON (AS SUCROSE) 100 MG/5 ML INJECTION, 5 X 5 ML AMPOULES	1	5	Venofer	AS

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Iron deficiency anaemia
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Treatment criteria:	Patient must be undergoing chronic haemodialysis.
Clinical criteria:	The treatment must be in combination with an erythropoiesis stimulating agent, AND Patient must have had a documented hypersensitivity reaction to iron polymaltose, AND Patient must be a person in whom continued intravenous iron therapy is appropriate.

4 Clinical place for the current therapy

- 4.1 Iron sucrose is currently positioned as second-line therapy after iron polymaltose through the current PBS clinical criteria of ‘Patient must have had a documented hypersensitivity reaction to iron polymaltose’. The minor submission proposed to position iron sucrose as an alternative first-line treatment to iron polymaltose by removing the requirement to have a documented hypersensitivity reaction to iron polymaltose from the PBS restriction.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

5 Comparator

- 5.1 The minor submission nominated iron polymaltose as the main comparator.

For more detail on PBAC's view, see section 7 "PBAC outcome"

6 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Clinical Trials

- 6.3 The minor submission's literature search did not identify any clinical trials that would allow for a direct or indirect assessment of comparative efficacy and safety with the main comparator, iron polymaltose.
- 6.4 The minor submission identified the following clinical trials involving the use of iron sucrose in patients undergoing haemodialysis and receiving an erythropoiesis stimulating agent:

Trials and associated reports presented in the re-submission

Trial ID/First author	Protocol title/Publication title	Publication citation
Supplementary randomised trial		
Al-Momen	Clinical Study Report: Enhancement of rHuEPO effect by iron saccharate in haemodialysis patients.	1999
Hussein	Experience of iron saccharate supplementation in haemodialysis patients treated with erythropoietin.	<i>Nephrology</i> , 1998; 4, 105-108.
Kosch	A randomized, controlled parallel-group trial on efficacy and safety of iron sucrose (Venofer) vs iron gluconate (Ferrlecit) in haemodialysis patients treated with rHuEpo.	<i>Nephrology Dialysis Transplantation</i> , 2001; 16(6):1239-44.
Li & Wang	Intravenous iron sucrose in Chinese hemodialysis patients with renal anemia.	<i>Blood Purification</i> , 2008; 26(2):151-6.

Source: Minor submission, pages 22 and 35.

- 6.5 In the absence of direct and indirect comparisons between iron sucrose and iron polymaltose, the minor submission further cited treatment guidelines and review articles.

For more detail on PBAC's view, see section 7 "PBAC outcome"

Comparative effectiveness and harms

- 6.6 Comparative efficacy and safety data against iron polymaltose was not presented.
- 6.7 The PBAC had previously considered that iron sucrose is unlikely to demonstrate a therapeutic profile that can be distinguished from iron polymaltose. (November 2004 PBAC minutes, para 5.10.6).

For more detail on PBAC's view, see section 7 "PBAC outcome"

Clinical claim

- 6.8 The minor submission claimed that all available intravenous iron formulations are roughly equi-effective at a ratio of 1:1 per mg basis albeit with contrasting safety profiles.

For more detail on PBAC's view, see section 7 "PBAC outcome"

Economic analysis

- 6.9 Although the minor submission did not present a formal economic comparison, the clinical claim was consistent with a cost-minimisation analysis and an equi-effective dose of 1:1 elemental iron content was proposed. The equi-effective doses were not derived directly from trial-based evidence – rather, they were based on the observation that treatment guidelines and a Cochrane review did not distinguish dosing differences between the various iron formulations.
- 6.10 The PBAC had previously agreed that iron sucrose and iron polymaltose are equi-effective on a per mg elemental iron basis (November 2004 PBAC minutes, para 5.10.6).

For more detail on PBAC's view, see section 7 "PBAC outcome"

Estimated PBS usage & financial implications

- 6.11 The minor submission estimated a small net saving to the PBS of less than \$10 million per year in Year 5 of listing, with a total net saving to the PBS of less than \$10 million per year over the first 5 years of the amended listing. This is due to the savings achieved through the price reduction. This is summarised in the table below.

Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated extent of use					
Number treated ^a	██████	██████	██████	██████	██████
Market share ^b	██████	██████	██████	██████	██████
Utilisation – max quantities (5 x 100mg/5mL) dispensed ^c	██████	██████	██████	██████	██████
Estimated net cost to PBS/RPBS					
Additional cost of iron sucrose	██████	██████	██████	██████	██████
Decreased cost of iron sucrose and use of polymaltose	██████	██████	██████	██████	██████
Total net cost to PBS/RPBS	██████	██████	██████	██████	██████

^a Assuming: annual growth in patients on haemodialysis of █████; that █████ of haemodialysis patients use erythropoietin stimulating agent and are eligible for iron sucrose; █████ of eligible patients currently use iron sucrose; all patients currently receiving iron sucrose will continue; and substitution of iron polymaltose to iron sucrose of █████ in Year 1 to █████ in Year 5.

^b Calculated by Secretariat: Total IS patients/Eligible IS population (Table 3.2).

^c Assuming █████ PBS Max Qty. per patient per year (or █████ vials per patient per year) as estimated by the submission.
Source: Tables 3.1, 3.2, 3.3 and 3.4 pp 29 and 32-34 of the submission and the Financial Workbook.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

7 PBAC Outcome

- 7.1 The PBAC recommended amending the current listing of iron sucrose to be identical to iron polymaltose, on a cost-minimisation basis with iron polymaltose. The PBAC considered that iron sucrose and iron polymaltose are equi-effective on a per mg elemental iron basis.
- 7.2 The PBAC accepted the nominated comparator of iron polymaltose.
- 7.3 The PBAC recalled that iron sucrose was recommended for listing in November 2004, as an Authority Required benefit on the basis of acceptable cost effectiveness in patients who have failed prior IV iron polymaltose therapy due to hypersensitivity reactions, noting the substantial price difference between the two products at the time. The PBAC further recalled that it had previously considered in November 2004 that iron sucrose is unlikely to demonstrate a therapeutic profile that can be distinguished from iron polymaltose and had previously agreed that iron sucrose and iron polymaltose are equi-effective on a per mg elemental iron basis. Given that the sponsor of iron sucrose was now proposing price-parity between iron polymaltose and iron sucrose, the PBAC considered it reasonable that iron sucrose’s restriction be identical to iron polymaltose’s restriction.
- 7.4 The PBAC noted that since the time of lodgement of the minor submission, the price of iron polymaltose had further reduced from 1 October 2014 as a result of statutory price disclosure measures.
- 7.5 The PBAC further noted that iron (as ferric carboxymaltose) had been recommended on a cost minimisation basis with iron polymaltose in March 2013 and again following resubmission in November 2013. Listing was effective on 1 June 2014 and the Department had been requested to calculate a cost-minimisation price for iron (as ferric carboxymaltose) that accounts for the advantages in reduced administration time compared to iron polymaltose. Since iron sucrose would have the same

advantage, the PBAC considered that it would be appropriate for the Department to review the price of iron (as ferric carboxymaltose).

7.6 The PBAC noted that the submission is not eligible for an Independent Review.

Outcome:

Recommended

8 Recommended listing

8.1 *Add the following new unrestricted benefit listing:*

Name, Restriction, Manner of administration and form	Max. Qty (packs)	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
IRON SUCROSE Iron (as sucrose) 100 mg /5 mL injection, 5 x 5 mL ampoules	1	5	..	Venofer AS

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction level:	Unrestricted

Amend the existing listing to appear as follows:

Name, Restriction, Manner of administration and form	Max. Qty (packs)	Max. Qty (units)	No. of Rpts	Proprietary Name and Manufacturer
IRON SUCROSE Iron (as sucrose) 100 mg /5 mL injection, 5 x 5 mL ampoules	1	5	5	Venofer AS

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Iron deficiency anaemia (4302)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input checked="" type="checkbox"/> Streamlined
Treatment criteria:	Patient must be undergoing chronic haemodialysis.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

10 Sponsor's Comment

Aspen Pharmacare welcomes the recommendation to expand the listing of Venofer[®]. The expanded listing creates broader access for patients undergoing haemodialysis, as aligned with the Product Information. The listing will not alter the administration advantage of ferric carboxymaltose compared to iron polymaltose, as determined in the November 2013 PBAC meeting.