

An addendum to this minute has been included at the end of the document.

5.14 FERRIC DERISOMALTOSE

**Injection 1000 mg (iron) in 10 mL,
Injection 500 mg (iron) in 5 mL,
Monofer[®], Pfizer Australia Pty Ltd.**

1 Purpose of Application

- 1.1 The minor submission requested a Section 85 General Schedule, Unrestricted listing for ferric derisomaltose (Monofer[®]) 1000 mg in 10 mL solution for injection.
- 1.2 Additionally, the submission requested a revision to the current PBS listing for ferric derisomaltose (Monofer[®]) 500 mg in 5 mL solution for injection.

2 Requested listing

- 2.1 The requested listings are shown below. Changes proposed in the submission are shown in bold text.

New listing requested:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
FERRIC DERISOMALTOSE IRON (AS FERRIC DERISOMALTOSE) 1000 MG/10 ML INJECTION, 10 ML VIAL	1	1	Published: \$307.73	Monofer [®]	Pfizer Australia Pty Ltd

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
Administrative Advice	Special Pricing Arrangements apply.

Amendments to PBS Item 11615H:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
FERRIC DERISOMALTOSE IRON (AS FERRIC DERISOMALTOSE) 500 MG/5 ML INJECTION, 5 ML VIAL	23	40	Published: \$459.06	Monofer®	Pfizer Australia Pty Ltd

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
Administrative Advice	Special Pricing Arrangements apply.

2.2 The submission requested to list a new strength of ferric derisomaltose, 1000 mg/10 mL solution for injection, to accommodate patients requiring a dose of 1000 mg. The submission requested a maximum quantity and maximum repeat of 1. The request for 1 repeat was to allow a maximum iron dose of 2000 mg to be administered as two doses, as the maximum permissible dose that can be administered in a single infusion is 1500 mg per week. This dose in line with the simplified dosing table (Table 1).

Table 1: The cumulative iron need using the simplified dosing table for ferric derisomaltose

Hb (g/L)	Patients with a bodyweight 50kg to <70kg	Patients with body weight ≥ 70 kg
≥ 100	1000 mg	1500 mg
< 100	1500 mg	2000 mg

Source: TGA approved product information for ferric derisomaltose (p2). Abbreviations: Hb = haemoglobin

2.3 The submission also requested a revision of the current listing of ferric derisomaltose 500 mg/5 mL vial (PBS Item 11615H) to provide a quantity that is consistent with the maximum permissible dose of 1500 mg that can be administered in a single infusion (i.e. 500 mg x 3 vials). The submission requested an increase to the maximum quantity from 2 to 3; and a reduction in the number of repeats from 1 to 0. This amendment would allow patients to receive the maximum quantity of 1500 mg per prescription. The submission noted that prescribers can currently apply for an authority to prescribe greater quantities than the current listing. However, the submission argued that amending the current listing to allow for the greater quantity would reduce the administrative burden and allow faster access for patients who require an iron dose of more than 1000 mg. The submission also claimed that ferric derisomaltose has the potential to reduce the number of intravenous infusions required, wastage, and number of doctor visits, because it can be administered at a higher dose in a single infusion (maximum dose of 1500 mg per week) when compared to ferric carboxymaltose (maximum dose of 1000 mg per week).

3 Background

- 3.1 Ferric derisomaltose is an intravenous (IV) iron, suitable for fast infusion and administration in primary care and other non-hospital settings.
- 3.2 The ferric derisomaltose 500 mg/5mL vial was TGA registered on 4 December 2017 and the 1000 mg/10 mL vial was registered on 13 November 2018. The TGA indication for both presentations is for the treatment of iron deficiency in adults, under the following conditions:
- When oral iron preparations are ineffective or cannot be used; or
 - Where there is a clinical need to deliver iron rapidly.

The diagnosis must be based on laboratory tests.

- 3.3 At its July 2018 meeting, the PBAC recommended the listing of ferric derisomaltose 500 mg/5mL vial as a Section 85 General Schedule, Unrestricted listing. The PBAC recommended the listing on a cost-minimisation basis with ferric carboxymaltose (paragraph 7.1, ferric derisomaltose Public Summary Document (PSD), July 2018). Ferric derisomaltose was listed on the PBS in February 2019.
- 3.4 There are three other PBS listed IV iron formulations: iron polymaltose, iron sucrose and ferric carboxymaltose. Iron polymaltose is required to be infused over a five hour period and would therefore not be suitable for administration in a non-hospital settings. However, patients treated with iron polymaltose may receive up to 2500 mg of iron in a single infusion. Iron sucrose is administered during dialysis and is TGA registered for use in patients undergoing haemodialysis and receiving erythropoietin stimulating agents. In comparison, ferric carboxymaltose is a fast-infusion iron formulation that can be administered in a single infusion up to 1000 mg in 20 minutes once a week, and would therefore be suitable for administration in non-hospital settings (paragraph 5.2, ferric derisomaltose PSD, July 2018).

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Clinical trials

- 4.3 As a minor submission, no clinical trials were presented in the submission.

Economic analysis

4.4 As a minor submission, no economic comparison was presented in the submission.

Drug cost/patient/course

4.5 The submission proposed an equivalent price per milligram for the 1000 mg/10 mL vial relative to the 500 mg/5 mL vial. This is consistent with the July 2018 consideration of ferric derisomaltose, where ferric derisomaltose was recommended to have the same overall cost of treatment as ferric carboxymaltose, with a published approved ex-manufacture price (AEMP) of \$272 per 1000 mg, assuming an equi-effective dose of 1 mg (ferric derisomaltose): 1 mg (ferric carboxymaltose) (paragraph 6.38, ferric derisomaltose PSD, July 2018).

4.6 Based on the proposed published Dispensed Price for Maximum Quantity (DPMQ) of \$307.73 for 1000 mg/10 mL vial (maximum quantity of 1 vial) and \$459.06 for 500 mg/5 mL (maximum quantity of 3 vials) of ferric derisomaltose, the cost per patient per course of treatment with ferric derisomaltose for the following doses is:

- 1000 mg dose (the most commonly prescribed dose based on the 2017 DUSC utilisation review) = \$307.73;
- 1500 mg dose = \$459.06 (based on 3 vials of the 500 mg/mL); and
- 2000 mg dose = \$615.26 (based on 2 vials of 1000 mg/10 mL).

4.7 Based on the proposed effective DPMQ of \$ [REDACTED] for 1000 mg/10 mL vial (maximum quantity of 1 vial) and \$ [REDACTED] for 500 mg/5 mL (maximum quantity of 3 vials) of ferric derisomaltose, the effective cost per patient per course of treatment with ferric derisomaltose for the following doses is:

- 1000 mg dose (the most commonly prescribed dose based on the 2017 DUSC utilisation review) = \$ [REDACTED];
- 1500 mg dose = \$ [REDACTED] (based on 3 vials of 500 mg/5 mL);
- 2000 mg dose = \$ [REDACTED] (based on 2 vials of 1000 mg/10 mL).

Estimated PBS usage & financial implications

4.8 Table 2 presents PBS data for the number of vials of ferric derisomaltose 500 mg/5 mL supplied per dispensing since listing on 1 February 2019. Based on three months of data, the majority of patients (87%) required a dose of 1000 mg of ferric derisomaltose (2 vials of 500 mg/5 mL). Around 9% of patients required a single vial dose of 500 mg, and 4% required a dose of 1500 mg (3 vials of 500 mg/5 mL). As there was a small number of patients requiring an iron dose of 1500 mg, the submission's claim that there will be reduced wastage as a result of the amendment to the 500 mg/5 mL listing will likely be minimal.

Table 2: Number of ferric derisomaltose 500 mg/5 mL vials supplied per dispensing

No. of vials supplied at dispensing	Proportion of patients#
1	9.2%
2	86.8%
3	4.0%

#Department of Human Services (DHS) Prescription database for the period from 1 February 2019 to 30 April 2019 inclusive, based on the date that the prescription was supplied.

4.9 Table 3 presents the number of ferric derisomaltose vials supplied per month since listing on 1 February 2019. Table 4 presents the market share of PBS-listed parenteral iron preparations based on number of prescriptions. The data shows that although the ferric derisomaltose market is small, it has been growing since being listed from 1 February 2019.

Table 3: Number of ferric derisomaltose 500 mg/5 mL prescriptions supplied per month

Month of Supply	Total no. of prescriptions#
February 2019	10
March 2019	29
April 2019	37

#Department of Human Services (DHS) Prescription database for the period from 1 February 2019 to 30 April 2019 inclusive, based on the date that the prescription was supplied.

Table 4: Market share of PBS-listed parenteral iron preparations based on number of prescriptions

Drug	Total no. prescriptions (% of total)#
Ferric carboxymaltose	285,052 (92%)
Iron polymaltose complex	21,685 (7%)
Iron sucrose	3,457 (1%)
Ferric derisomaltose	76 (<1%)*

#Department of Human Services (DHS) Prescription database for the period from 1 May 2018 to 30 April 2019 inclusive, based on the date that the prescription was supplied.

*Ferric derisomaltose listed on 1 February 2019.

4.10 The submission claimed that, according to an audit conducted in the United Kingdom (Kearns et al, 2018), 18% of patients received less iron (ferric derisomaltose) than the amount stated in the simplified dosing table. The submission attributed the under-dosage to the 'habit' of prescribing the maximum permissible dose of 1000 mg ferric carboxymaltose per infusion because prescribers were not aware of the maximum dosage of 1500 mg for ferric derisomaltose. The submission stated that there is currently a prescriber education program around the appropriate dosing with ferric derisomaltose using the simplified dosing table. The pre-PBAC response clarified the prescriber education program consists of various activities to increase awareness of the dosing regimen for ferric derisomaltose with the aim to change prescribing habits.

- 4.11 The submission did not present financial data. The submission stated that it did not anticipate that the change to the current listing or the listing of a new strength of ferric derisomaltose would significantly change the overall usage of ferric derisomaltose on the PBS.

Financial management – Risk Share Arrangements and Special Pricing Arrangements

- 4.12 The submission noted that ferric derisomaltose is subject to a Deed of Agreement (the Deed) for IDA; ferric carboxymaltose is also subject to this Deed. The Deed encompassed a Special Pricing Arrangement (SPA) rebate and subsidisation cap arrangement. At the time of PBAC consideration, the nominal term of the Deed had expired.
- 4.13 In March 2017, the PBAC considered the February 2017 DUSC report on ferric carboxymaltose and noted that the predicted versus actual use of ferric carboxymaltose was substantially higher in the first 24 months since its PBS listing on 1 June 2014 (Consideration of DUSC Report web outcome, PBAC March 2017 meeting). The PBAC also noted that:
- ferric carboxymaltose received a higher market share than anticipated but its listing also led to substantial growth in the injectable iron market;
 - available data were currently insufficient to assess the extent of any shift from oral iron to ferric carboxymaltose on the basis of preference, but considered that use in this setting has not been assessed for cost-effectiveness;
 - management of iron levels prior to surgery has been promoted to reduce the use of blood transfusions;
 - use in the dialysis population does not seem to be a concern at present and could be reassessed in any subsequent review; and
 - variation in the use of ferric carboxymaltose across Australia may reflect educational activities and infusion programs or clinics in those areas with more use.
- 4.14 In July 2018, the PBAC considered that the listing of ferric derisomaltose was not likely to expand the IV iron market in terms of patient numbers beyond that estimated in the July 2018 submission. However, the PBAC noted that the maximum dose per IV infusion for ferric derisomaltose (1500 mg) is higher than that of ferric carboxymaltose (1000 mg). The PBAC considered that listing may result in a rise in the most commonly prescribed dose from the 1000 mg reported in the 2017 DUSC utilisation review, as clinicians are likely to use the simplified dosing regimen. The PBAC considered that this might lead to higher than expected use of ferric derisomaltose, and recommended that DUSC undertake a review of utilisation after an appropriate period post listing (paragraph 7.6, ferric derisomaltose PSD, July 2018).

- 4.15 As the Deed for IDA is expired, the new term will need to be renegotiated between the Department and the sponsors of ferric carboxymaltose and ferric derisomaltose. The PBAC considered that a Risk Sharing Arrangement (RSA) continued to be necessary as any shift from oral iron preparations to ferric derisomaltose and ferric carboxymaltose due to patient preference has not been considered as cost-effective. The PBAC further considered that it would be appropriate for a new RSA to be implemented based on the same forward estimates projections and similar derivation of the RSA Caps as the original RSA. Once such an RSA is implemented, the ferric derisomaltose 1000 mg/10 mL could be included under the arrangement and would need to be cost neutral to the health system overall to be considered cost effective.
- 4.16 At the time of the original recommendation of ferric derisomaltose in July 2018, the PBAC noted that the sponsor was willing to adopt a SPA equivalent to that of the main comparator, ferric carboxymaltose, to ensure the cost-minimisation framework was maintained (paragraph 7.8, ferric derisomaltose PSD, July 2018). The submission acknowledged that the 1000 mg/10 mL vial would also be subject to this agreement.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC deferred making a recommendation on the unrestricted Section 85 listing for ferric derisomaltose 1000 mg/10 mL and the change to maximum quantity and repeats for ferric derisomaltose 500 mg/10 mL. However, the PBAC was of the mind to recommend the request for a new strength of ferric derisomaltose, 1000 mg/10 mL solution for injection and the requested changes to the maximum quantity and repeats for the current listing of the 500 mg/5 mL vial of ferric derisomaltose. The PBAC deferred making a decision pending the outcomes from the renegotiation of a new term for the Deed of Agreement for iron deficient anaemia (IDA), which applies to ferric carboxymaltose and ferric derisomaltose.
- 5.2 The PBAC maintained its view that the clinical place for ferric derisomaltose would remain as an alternative IV iron formulation for the treatment of iron deficiency anaemia when treatment with oral iron is ineffective or not tolerated (paragraph 7.2, ferric derisomaltose PSD, July 2018).
- 5.3 The PBAC noted that the additional strength and change to the current listing of ferric derisomaltose aligned with the TGA registration.
- 5.4 The PBAC considered that the requested maximum quantity and maximum repeats for the 1000 mg vial strength to be appropriate. The PBAC noted that this would allow for the maximum iron dose of 2000 mg (administered as two doses as the maximum permissible dose is 1500 mg per week) to be prescribed in accordance with the simplified dosing table.
- 5.5 The PBAC considered the requested changes to the current listing of the 500 mg vial strength of ferric derisomaltose, including an increase of the maximum quantity to 3

- and a reduction in the number of repeats to 0, were appropriate. The PBAC noted that this change would allow for a maximum iron dose of 1500 mg dose to be prescribed.
- 5.6 The PBAC accepted an equivalent price per milligram for the 1000 mg/10 mL vial relative to the 500 mg/5 mL vial. This was consistent with the July 2018 consideration of ferric derisomaltose where ferric derisomaltose was recommended to have the same overall cost of treatment as ferric carboxymaltose with a published approved ex-manufacture price (AEMP) of \$272 per 1000 mg, assuming an equi-effective dose of 1 mg (ferric derisomaltose): 1 mg (ferric carboxymaltose) (paragraph 6.38, ferric derisomaltose PSD, July 2018).
- 5.7 The PBAC noted that there was currently limited PBS data for ferric derisomaltose as it was listed in early 2019. However, the PBAC considered that the ferric derisomaltose market is growing despite the current small market share.
- 5.8 The PBAC noted that the sponsor is implementing a prescriber education program around the appropriate dosing of ferric derisomaltose using the simplified dosing table. The aim of the program is to raise awareness of the recommended iron doses for ferric derisomaltose using the simplified dosing table, which ranges from 1000 mg – 2000 mg and is based on patient body weight and haemoglobin (Hb) targets. The PBAC considered that iron doses of 1000 mg may still be sufficient for many patients. However, the education program would change the prescribing behaviour and increase the use of the 1500 mg dose of ferric derisomaltose. The PBAC considered that this change will grow the overall market for infusible iron. The PBAC reiterated its recommendation from July 2018 that DUSC undertake a review of ferric derisomaltose utilisation after an appropriate period post listing.
- 5.9 The PBAC noted that ferric carboxymaltose and ferric derisomaltose were subject to a Risk Sharing Arrangement (RSA) for IDA. The PBAC noted that the nominal term for this Deed had expired. The PBAC considered that the subsidisation caps should be renegotiated to manage any ongoing risk of use outside the population for which both ferric carboxymaltose and ferric derisomaltose have been considered cost effective. The PBAC noted that the subsidisation caps for the Deed had been consistently exceeded from Year 2 given ferric carboxymaltose use was substantially higher in the first 24 months since its PBS listing on 1 June 2014. The PBAC considered the implementation of the prescriber education would likely contribute to higher than expected use of ferric derisomaltose, and would subsequently result in an overall growth of the infusible iron market. Additionally, the PBAC noted that there was currently insufficient data to assess the extent of any shift from oral iron to infusible iron on the basis of patient preference, and considered that use in this setting had not been assessed for cost-effectiveness. Therefore, in making its decision to defer, the PBAC considered that it would be appropriate for a new RSA to be implemented based on the same forward estimates projections and similar derivation of the RSA Caps as in the original RSA, and that the new agreement should capture both ferric carboxymaltose and ferric derisomaltose use. Once such an RSA is implemented, the ferric derisomaltose 1000 mg/10 mL could be included under the arrangement and

would need to be cost neutral to the health system overall to be considered cost effective. The PBAC noted that it would be open to the sponsors of these medicines to put forward an alternative proposal that addresses cost-effectiveness in patients who might move from oral iron to these agents due to preference, but that it had no basis to consider this broader use as cost-effective at this time. The PBAC considered the outcomes of the Deed negotiation would need to be resolved before making a recommendation for the ferric derisomaltose listing.

Outcome:

Deferred

6 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.

7 Sponsor's Comment

The sponsor had no comment.

August 2019 addendum to the July 2019 PBAC Minutes:

8 Purpose of Application

- 8.1 At its July 2019 meeting, the PBAC deferred making a recommendation regarding the listing of ferric derisomaltose pending the outcomes from the renegotiation of a new term for the Deed of Agreement (the Deed) for iron deficient anaemia.
- 8.2 Since the meeting, the Department clarified that the existing Deed for ferric derisomaltose does not specify the form of the drug, and if PBS-listed, would be subject to the existing arrangements under the Deed. Accordingly, utilisation of the new form of ferric derisomaltose, 1000 mg/10 mL would be included under the subsidisation caps under the existing Deed.

9 PBAC Outcome

- 9.1 The PBAC recommended the unrestricted listing of a new form of ferric derisomaltose, 1000 mg/10 mL solution for injection. The PBAC also recommended an increase of the maximum quantity to 3 and a reduction in the number of repeats to 0 for the current listing for ferric derisomaltose 500 mg/10 mL solution for injection.

- 9.2 The PBAC noted advice from the Department that while the nominal term for the existing Deed had expired, the Deed was not form specific and would remain in place, subject to the conditions of the last Year of the Deed, until it is replaced or terminated. Accordingly, the subsidisation caps under the existing Deed would apply to the new form of ferric derisomaltose, 1000 mg/10 mL, and the listing would result in no additional cost to Government.
- 9.3 The PBAC considered that ferric derisomaltose should not be treated as interchangeable with any other drugs.
- 9.4 The PBAC considered that ferric derisomaltose is suitable for prescribing by nurse practitioners.
- 9.5 The PBAC considered that the Early Supply Rule should not apply.
- 9.6 The PBAC noted that this submission was not eligible for Independent Review as it received a positive recommendation.

Outcome:

Recommended

10 Recommended listing

10.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
FERRIC DERISOMALTOSE IRON (AS FERRIC DERISOMALTOSE) 1000 MG/10 ML INJECTION, 10 ML VIAL	1	1	Monofer®	Pfizer Australia Pty Ltd
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			
Administrative Advice	Special Pricing Arrangements apply.			

10.2 Make the following changes to PBS Item 11615H:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
FERRIC DERISOMALTOSE IRON (AS FERRIC DERISOMALTOSE) 500 MG/5 ML INJECTION, 5 ML VIAL	23	40	Monofer®	Pfizer Australia Pty Ltd
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			
Administrative Advice	Special Pricing Arrangements apply.			

11 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.

12 Sponsor's Comment

The sponsor had no comment.