

7.14 ERTUGLIFLOZIN

**Tablet containing 15 mg ertugliflozin,
Steglatro®;**

ERTUGLIFLOZIN with METFORMIN

**Tablet containing 7.5 mg ertugliflozin with 500 mg
metformin hydrochloride,**

**Tablet containing 7.5 mg ertugliflozin with 1 g
metformin hydrochloride,**

Segluromet®,

Merck Sharp & Dohme (Australia) Pty Ltd.

1 Purpose of Application

- 1.1 The minor resubmission requested an Authority Required (STREAMLINED) listing for the higher strength formulations of ertugliflozin (15 mg), as a single agent, and ertugliflozin with metformin (7.5 mg/500 mg, 7.5 mg/1 g), as fixed dose combination (FDC) products, for patients with Type 2 diabetes mellitus who are inadequately controlled with metformin or a sulfonylurea.

2 Requested listing

- 2.1 The proposed listings were the same as those recommended by the PBAC in March 2018 for the lower strength ertugliflozin products. However, as per the PBS listing of dapagliflozin and empagliflozin on 1 April 2018 for use as triple therapy, the submission requested that the note precluding use with a dipeptidyl peptidase-4 (DPP4) inhibitor (gliptin) be deleted.

Name, Restriction, Manner of administration and Form	Max. qty packs	No. of repeats	DPMQ	Proprietary Name and Manufacturer	
ERTUGLIFLOZIN <i>ertugliflozin 15 mg tablet, 28</i>	1	5	\$58.27	Steglatro®	Merck Sharp & Dohme (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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined

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Clinical criteria:	<p>The treatment must be in combination with metformin; OR The treatment must be in combination with a sulfonylurea, AND Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with either metformin or a sulfonylurea; OR Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with either metformin or a sulfonylurea.</p>
Administrative Advice	<p>Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>This drug is not PBS subsidised for use as monotherapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.</p>

Name, Restriction, Manner of administration and Form	Max. qty packs	No. of repeats	DPMQ	Proprietary Name and Manufacturer
ERTUGLIFLOZIN + METFORMIN				
<i>ertugliflozin 7.5 mg + metformin 500 mg tablet, 56</i>	1	5	\$59.78	Segluromet® Merck Sharp & Dohme (Australia) Pty Ltd
<i>ertugliflozin 7.5 mg + metformin 1 g tablet, 56</i>	1	5	\$61.18	

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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Treatment phase:	Initial treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with metformin; OR Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with metformin.</p>
Administrative Advice	<p>This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.</p>

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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	Patient must have previously received and been stabilised on a PBS-subsidised regimen of oral diabetic medicines which includes metformin and ertugliflozin.
Administrative Advice	Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners. This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.

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

3 Background

- 3.1 A major submission was considered at the March 2018 PBAC meeting for ertugliflozin as a single agent (5 mg and 15 mg) and in combination with metformin (2.5 mg/500mg, 2.5 mg/1 g, 7.5 mg/500 mg and 7.5 mg/1 g).
- 3.2 At the March 2018 meeting the PBAC recommended ertugliflozin 5 mg and the related FDC products, ertugliflozin with metformin 2.5 mg/500 mg and 2.5 mg/1 g, for listing on the PBS.
- 3.3 Ertugliflozin 15 mg and the related FDC products, ertugliflozin with metformin 7.5 mg/500 mg and 7.5 mg/1 g, were not recommended for listing as:
- at the time of consideration a positive TGA Delegate's Overview was not received for the ertugliflozin 15 mg dose (and its related products); and
 - the evidence provided in the submission did not support the clinical need for the higher strength products, especially given the doubt as to the non-inferior safety profile compared to their respective comparators [paragraph 7.4, 5.03 PBAC March 2018 Public Summary Document (PSD)].
- 3.4 A positive recommendation from the TGA's ACM was received for all strengths and formulations of ertugliflozin on 16 April 2018.
- 3.5 The approved indication for ertugliflozin and ertugliflozin with metformin FDC products was:
- “as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus as:
- monotherapy when metformin is considered inappropriate due to intolerance; or

- in combination with other anti-hyperglycaemic agents”.
- 3.6 Ertugliflozin with sitagliptin (5 mg/100 mg and 15 mg/100 mg) FDC products were considered and recommended by the PBAC as a major submission at the July 2018 meeting.

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

4 Population and disease

- 4.1 The submission positioned ertugliflozin as an alternative to other SGLT2 inhibitors, dapagliflozin and empagliflozin, for dual oral therapy with concurrent metformin or a sulfonylurea to treat Type 2 diabetes mellitus in patients with inadequate glycaemic control, defined by glycosylated haemoglobin levels (HbA1c) > 7.0%, despite treatment with metformin or a sulfonylurea.

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 No new clinical trials were presented in the resubmission. Some new evidence, which was presented to the TGA, was provided.

Comparative effectiveness

- 5.4 The March 2018 PBAC decision did not support the clinical need for the higher strength ertugliflozin products as no direct evidence was provided to indicate that there were improved outcomes from an increase in dose [paragraph 7.9, 5.03 PBAC March 2018 PSD].
- 5.5 The minor resubmission stated that the evidence provided in the original submission demonstrated that both strengths of ertugliflozin met the non-inferiority threshold of 0.4% change in HbA1c in comparison to all strengths of the comparators, and that the results were statistically significant in favour of ertugliflozin 15 mg.
- 5.6 The resubmission re-presented the results from the placebo-controlled indirect comparison.

Table 1: Summary results of the indirect comparison of change in HbA1c from baseline with ertugliflozin, dapagliflozin and empagliflozin at 24/26 weeks

Change in HbA1c from baseline (mean difference (95% CI), negative results favour ertugliflozin)	
Comparison	Placebo reference
ERTU 5 mg versus DAPA 10 mg	-0.21 (-0.47, 0.05)
ERTU 5 mg versus EMPA 10 mg	-0.13 (-0.35, 0.09)
ERTU 5 mg versus EMPA 25 mg	-0.06 (-0.28, 0.16)
ERTU 15 mg versus DAPA 10 mg	-0.39 (-0.65, -0.13)
ERTU 15 mg versus EMPA 10 mg	-0.31 (-0.54, -0.08)
ERTU 15 mg versus EMPA 25 mg	-0.24 (-0.47, -0.01)

Source: Table 1, p4 of the resubmission

CI = confidence interval; DAPA = dapagliflozin; EMPA = empagliflozin; ERTU = ertugliflozin; HbA1c = glycated haemoglobin

- 5.7 In terms of change from baseline in HbA1c, the differences between the treatments in the primary indirect analysis (with placebo as a common reference) did not exceed that nominated non-inferiority margin of 0.4%. Ertugliflozin 15 mg demonstrated statistical superiority over dapagliflozin and empagliflozin.
- 5.8 Data from over 1,500 patients from three Phase III placebo-controlled trials (PBO Pool) were presented to the TGA comparing the efficacy of both doses of ertugliflozin with placebo in the intended population.

Table 2: HbA1c (%) change from baseline at Week 26, PBO Pool (Full analysis set)

	N	HbA1c change from baseline, % (SD)	LS mean (95% CI)	LSMD (95% CI)
Placebo	515	-0.15 (0.93)	0.00 (-0.08, 0.08)	-
Ertugliflozin 5 mg	519	-0.77 (0.87)	-0.76 (-0.84, -0.68)	-0.76 (-0.87, -0.65)
Ertugliflozin 15 mg	509	-0.95 (0.92)	-0.91 (-0.99, -0.83)	-0.91 (-1.02, -0.80)

Source: Table 2, p5 of the resubmission

CI = confidence interval; HbA1c = glycated haemoglobin; LS = least squares; LSMD = least squares mean difference; SD = standard deviation

- 5.9 Although the studies were not powered to demonstrate a difference between doses, ertugliflozin 15 mg resulted in an incremental HbA1c reduction of 0.15% relative to ertugliflozin 5 mg.
- 5.10 At the ACM the TGA noted that the 0.15% incremental reduction was only modest and not clinically significant, and that the mean effect was small and it might only have limited use in clinical practice.
- 5.11 The minor submission also noted that the PBAC has previously recommended both the lower and higher strength formulations of empagliflozin (10 mg, 25 mg) despite there being no evidence of a statistically significant benefit associated with the higher strength.

Comparative harms

- 5.12 A detailed outline of the pre-ACM response addressed the following safety concerns which were outlined in the TGA Delegate's Overview:
- That there was a higher rate of adverse events when comparing the 15 mg strength to the 5 mg strength.

- In the PBO Pool the overall percentage of patients with one or more adverse events was 51.1% in the placebo group, 45.5% in the ertugliflozin 5 mg group and 50.4% in the ertugliflozin 15 mg group.
- The incidence of non-fatal serious adverse events was 2.9%, 3.3% and 2.4% in the placebo, ertugliflozin 5 mg and ertugliflozin 15 mg groups respectively.
- Whether there was a cardiovascular risk and the incidence of cardiovascular events between the lower and higher doses of ertugliflozin.
 - Data from the 4-month Safety Update Report (SUR) showed similar incidences of non-fatal serious adverse events in the cardiac disorders category – placebo: 1.0%; ertugliflozin 5 mg: 1.5%; and ertugliflozin 15 mg: 1.4%.
 - Analysis of cardiovascular events across the development program showed the incidence was similar across groups (4.4%, 4.2% and 2.8% in the placebo, ertugliflozin 5 mg and ertugliflozin 15 mg groups respectively).
- The incidences of volume depleting and renal adverse events with ertugliflozin 15 mg compared to those reported with the higher strengths of other SGLT2 inhibitors.
 - The incidence of volume depletion in the PBO Pool was 1.7%, 0.8% and 1.0% in the placebo, ertugliflozin 5 mg and ertugliflozin 15 mg groups respectively. With respect to other SGLT2 inhibitors, the incidence of volume depletion was 1.3%, 0.4% and 1.1% for the high doses of canagliflozin, empagliflozin and dapagliflozin respectively.
 - The incidence of renal related adverse events in the Broad Pool (including subjects with moderate renal impairment) was 0.4%, 0.6% and 0.8% in the placebo, ertugliflozin 5 mg and ertugliflozin 15 mg groups. For other SGLT2 inhibitors the incidence was 0.9%, 1.3% and 4.0% for the high doses of canagliflozin, empagliflozin and dapagliflozin respectively.

5.13 The ACM minutes noted:

- That there were more adverse events with the 15 mg strength;
- That the incidences of volume depletion and renal adverse events with ertugliflozin 15 mg were not higher than those reported with the higher strengths of other SGLT2 inhibitors; and
- The additional cardiovascular data provided was reassuring and that registration should not be denied on the absence of long term cardiovascular outcomes.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required (STREAMLINED) listing of the 15 mg dose strength ertugliflozin for dual oral therapy with metformin or a sulfonylurea, and the 7.5 mg ertugliflozin with 500 mg metformin and 7.5 mg ertugliflozin with 1 g

metformin fixed dose combination (FDC) products, for the treatment of Type 2 diabetes mellitus in patients inadequately controlled with metformin or a sulfonylurea.

- 6.2 Following receipt of a positive TGA Delegate's Overview, and clinical justification for accepting the higher strength of ertugliflozin, the PBAC advised of its recommendation whilst noting that there remained a limited clinical need for the higher strength products.
- 6.3 The PBAC considered that the evidence presented in the minor resubmission supported a claim of non-inferior efficacy and safety for ertugliflozin 15 mg compared to dapagliflozin or empagliflozin. The PBAC considered that the equi-effective doses are ertugliflozin 5mg or 15 mg (once daily), and dapagliflozin 10 mg (once daily) or empagliflozin 10 mg or 25 mg (once daily).
- 6.4 The PBAC considered that the evidence presented in the submission supported a claim of non-inferior efficacy and safety for ertugliflozin with metformin FDC products (7.5 mg ertugliflozin with 500 mg metformin and 7.5 mg ertugliflozin with 1 g metformin) compared to the individual components. The PBAC considered that the FDC products in the included ertugliflozin studies met the pre-specified bioequivalence margins against the individual components. The equi-effective doses for the FDC products were considered to be equivalent to the same dose of individual components taken concomitantly.
- 6.5 The PBAC considered that as per the PBS listings of dapagliflozin and empagliflozin on 1 April 2018 for use as triple therapy, the note precluding use with a dipeptidyl peptidase-4 (DPP4) inhibitor (gliptin) could be deleted from the listings for both high and low doses of ertugliflozin and ertugliflozin with metformin FDC products.
- 6.6 The PBAC advised that, under subsection 101(3BA) of the *National Health Act 1953* ertugliflozin and ertugliflozin with metformin should be treated as interchangeable on an individual patient basis with dapagliflozin and empagliflozin, and their corresponding FDC products with metformin, respectively.
- 6.7 The PBAC advised that ertugliflozin and ertugliflozin with metformin FDC products are suitable for prescribing by nurse practitioners for continuing therapy only, consistent with the current PBS listings for other SGLT2 inhibitors.
- 6.8 The PBAC recommended that the Early Supply Rule should apply to ertugliflozin and ertugliflozin with metformin FDC products as the Early Supply Rule applies to the current PBS listings for other SGLT2 inhibitors.
- 6.9 The PBAC noted that this submission is not eligible for an Independent Review as it has received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new items as follows:

Name, Restriction, Manner of administration and Form	Max. qty packs	No. of repeats	Proprietary Name and Manufacturer	
ERTUGLIFLOZIN <i>ertugliflozin 15 mg tablet, 28</i>	1	5	Steglatro®	Merck Sharp & Dohme (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
Condition:	Diabetes mellitus type 2
PBS indication:	Diabetes mellitus type 2
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>The treatment must be in combination with metformin; OR The treatment must be in combination with a sulfonylurea, AND Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with either metformin or a sulfonylurea; OR Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with either metformin or a sulfonylurea.</p>
Prescriber instructions:	<p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p> <p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p> <p>A patient whose diabetes was previously demonstrated unable to be controlled with metformin or a sulfonylurea does not need to requalify on this criterion before being eligible for PBS-subsidised treatment with this drug.</p>

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Administrative advice:	<p>Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>This drug is not PBS subsidised for use as monotherapy or in combination with a thiazolidinedione (glitazone), insulin or a glucagon-like peptide-1.</p>
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Name, Restriction, Manner of administration and Form	Max qty packs	No. of repeats	Proprietary Name and Manufacturer
ERTUGLIFLOZIN + METFORMIN			
<i>ertugliflozin 7.5 mg + metformin 500 mg tablet, 56</i>	1	5	Segluromet® Merck Sharp & Dohme (Australia) Pty Ltd
<i>ertugliflozin 7.5 mg + metformin 1 g tablet, 56</i>	1	5	

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
Condition:	Diabetes mellitus type 2
PBS indication:	Diabetes mellitus type 2
Treatment phase:	Initial treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with metformin;</p> <p>OR</p> <p>Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with metformin.</p>
Prescriber instructions:	<p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p> <p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p> <p>A patient whose diabetes was previously demonstrated unable to be controlled with metformin does not need to requalify on this criterion before being eligible for PBS-subsidised treatment with this fixed dose combination.</p>
Administrative advice:	This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), insulin or a glucagon-like peptide-1.

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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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	Patient must have previously received and been stabilised on a PBS-subsidised regimen of oral diabetic medicines which includes metformin and ertugliflozin.
Administrative advice:	Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners. This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), insulin or a glucagon-like peptide-1.

7.2 Amend existing listings as follows:

Name, Restriction, Manner of administration and Form	Max. qty packs	No. of repeats	Proprietary Name and Manufacturer	
ERTUGLIFLOZIN ertugliflozin 5 mg tablet, 28	1	5	Steglatro®	Merck Sharp & Dohme (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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The treatment must be in combination with metformin; OR The treatment must be in combination with a sulfonylurea, AND Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with either metformin or a sulfonylurea; OR Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with either metformin or a sulfonylurea.

Prescriber Instructions	<p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p> <p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p> <p>A patient whose diabetes was previously demonstrated unable to be controlled with metformin or a sulfonylurea does not need to requalify on this criterion before being eligible for PBS-subsidised treatment with this drug.</p>
Administrative Advice	<p>Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>This drug is not PBS subsidised for use as monotherapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.</p>

Name, Restriction, Manner of administration and form	Max. qty packs	No. of repeats	Proprietary Name and Manufacturer	
ERTUGLIFLOZIN + METFORMIN				
<i>ertugliflozin 2.5 mg + metformin 500 mg tablet, 56</i>	1	5	Segluromet®	Merck Sharp & Dohme (Australia) Pty Ltd
<i>ertugliflozin 2.5 mg + metformin 1 g tablet, 56</i>	1	5		

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
Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Treatment phase:	Initial treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with metformin;</p> <p>OR</p> <p>Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with metformin.</p>

Prescriber Instructions	<p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p> <p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months.</p> <p>The results of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p> <p>A patient whose diabetes was previously demonstrated unable to be controlled with metformin does not need to requalify on this criterion before being eligible for PBS-subsidised treatment with this fixed dose combination.</p>
Administrative Advice	<p>This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.</p>

Category / Program	GENERAL – General Schedule (Code GE)
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Condition:	Diabetes mellitus type 2
PBS Indication:	Diabetes mellitus type 2
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	Patient must have previously received and been stabilised on a PBS-subsidised regimen of oral diabetic medicines which includes metformin and ertugliflozin.
Administrative Advice	<p>Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>This fixed dose combination is not PBS subsidised for use as initial therapy or in combination with a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin), insulin or a glucagon-like peptide-1.</p>

8 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.

9 Sponsor's Comment

The sponsor had no comment.