

## 7.11 ITRACONAZOLE 50 mg capsule, 60, Lozanoc®, Mayne Pharma International Ltd

### 1 Purpose of Application

- 1.1 The minor re-submission requested Authority Required (STREAMLINED) listing of itraconazole 50 mg capsule (Lozanoc®) for the same indications as the currently PBS-listed itraconazole 100 mg capsule (Sporanox®).

### 2 Requested listing

- 2.1 The submission sought the following new listings, in line with the indications of the current PBS-listing for itraconazole 100 mg.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5	\$ [REDACTED]	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Systemic aspergillosis
<b>PBS Indication:</b>	Systemic aspergillosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5	\$ [REDACTED]	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Systemic sporotrichosis
<b>PBS Indication:</b>	Systemic sporotrichosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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ITRACONAZOLE Capsule, 50mg, 60	1	5	\$ [REDACTED]	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Systemic histoplasmosis
<b>PBS Indication:</b>	Systemic histoplasmosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Disseminated pulmonary histoplasmosis infection
<b>PBS Indication:</b>	Disseminated pulmonary histoplasmosis infection
<b>Treatment phase:</b>	Treatment and maintenance therapy
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	Patients <i>must be diagnosed with acquired immunodeficiency syndrome (AIDS).</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model:</i> <i>For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Chronic pulmonary histoplasmosis infection
<b>PBS Indication:</b>	Chronic pulmonary histoplasmosis infection
<b>Treatment phase:</b>	Treatment and maintenance therapy
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	Patients <i>must be diagnosed with acquired immunodeficiency syndrome (AIDS).</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Oropharyngeal candidiasis
<b>PBS Indication:</b>	Oropharyngeal candidiasis
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	<i>Patient must be immunosuppressed.</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Oesophageal candidiasis
<b>PBS Indication:</b>	Oesophageal candidiasis
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	<i>Patient must be immunosuppressed.</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

### 3 Background

3.1 Itraconazole 50mg capsule (Lozanoc®) is TGA registered for the following indications:

#### Superficial mycoses

Itraconazole 50mg capsule is indicated if external treatment is not effective or not appropriate, for the treatment of the following fungal infections: dermatomycoses (e.g. tinea corporis, tinea cruris, tinea pedis, tinea manus, tinea unguium) and Pityriasis versicolour.

#### Systemic mycoses

Itraconazole 50mg capsule is indicated for the treatment of systemic mycoses, such as candidiasis, aspergillosis, and histoplasmosis.

Consideration should be given to official guidance on the appropriate use of antimycotic agents, and to the discussion of the pharmacodynamics properties.

3.2 Itraconazole 50mg capsule was previously considered at the November 2014 PBAC. The PBAC rejected the submission for the treatment of systemic mycoses for the following reasons:

- The data demonstrating comparative efficacy and safety were not provided in the submission. Accordingly, the PBAC could not recommend (under section 101(3) of the Act) that itraconazole be made available as a pharmaceutical benefit.
- The PBAC noted that while the TGA found that the 50 mg capsules were therapeutically equivalent to the currently listed 100 mg itraconazole capsules on appeal, a bioequivalence statement was not issued.
- The PBAC considered there would be a small risk of prescriber or patient confusion if itraconazole 50 mg were to be listed. That is, there is a risk that a patient may receive twice the dose intended by the prescriber.
- While the PBAC considered there may be a small advantage to adding an additional brand of itraconazole to the PBS, it did not consider there was a compelling clinical need for listing.
- The PBAC noted that the submission did not provide data demonstrating comparative efficacy and safety relative to the nominated comparator (itraconazole 100 mg). The PBAC recommended the sponsor address these concerns via a re-submission.
- The minor submission did not address estimated PBS usage or financial implications.

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

#### **4 Clinical place for the proposed therapy**

4.1 Itraconazole 50mg capsule is TGA approved for superficial and systemic mycoses indications. This minor re-submission requested listing for systemic mycoses only, as per the current PBS-listing for itraconazole 100 mg capsule.

4.2 The re-submission claimed that one 50 mg capsule of itraconazole (Lozanoc<sup>®</sup>) has a higher bioavailability than other itraconazole capsules and is not affected by gastric acid neutralizers/inhibitors. Itraconazole 50 mg is therapeutically equivalent to one 100 mg capsule of itraconazole. However, itraconazole 50mg and itraconazole 100mg are not considered interchangeable.

## 5 Comparator

- 5.1 The previous minor submission considered by the PBAC in November 2014 nominated itraconazole 100mg capsule as the main comparator. This was unchanged.

*For more details 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 and welcomed the input from health care professionals (3) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with itraconazole 50 mg including better absorption and less variability in measured blood concentrations. The PBAC also noted improved patient outcomes in both life threatening invasive fungal disease in hospitals as well as superficial fungal infections managed by general practitioners in primary care setting.

### Clinical trials

- 6.3 The re-submission was based on the bioavailability, pharmacokinetic, efficacy and safety studies. From the Australian perspective, the bioavailability studies presented include HGN007 and HGN008. Details of the studies presented in the re-submission are provided in the table below.

**Table 1: Study and associated reports presented in the re-submission**

Study ID	Protocol title/ Publication title	Publication citation
<b>Bioavailability studies</b>		
HGN008	Randomised, single-dose, open-label, two-treatment, four-period, replicate-design, crossover study to evaluate the bioequivalence of Lozanoc® and Sporanox® in individuals under fed conditions.	None provided
HGN007	Single-dose, open-label, four-way crossover, four-sequence study designed to compare the efficacy and safety of Lozanoc® (SUBACAP™-itraconazole) 50 mg capsules (test) and Sporanox® (itraconazole) 100 mg capsules (reference) under fed and fasted conditions.	March 2010
10850706	Randomised, multiple- dose, two-period, crossover to evaluate the bioequivalence of a test product at a dose of 100 mg compared with a dose of 200 mg of a reference product currently on the market under fed conditions.	August 2008
10850705	Randomised, multiple- dose, two-period, crossover to evaluate the bioequivalence of Lozanoc® (SUBACAP™) at a dose of 100 mg compared to a dose of 200 mg of Sporanox® under fed conditions.	August 2008

Study ID	Protocol title/ Publication title	Publication citation
CM2907	Randomised, balanced, open-label, four-way crossover – Fed. To determine dose-response under the different food intake conditions	June 2007
CM7300	Randomised, crossover - Fed and fasted. To determine the effect of food on bioavailability and to evaluate inter-subject variability	August 2008
CM6000	Randomised, balanced, open-label, four-way crossover – Fed. To determine the effect of food on bioavailability	March 2000
10850703	Randomised, single-dose, 4-treatment, 4-period, crossover to evaluate the relative bioavailability of Lozanoc® (SUBACAP™) at a dose of 50 mg and Sporanox® at a dose of 100 mg in a fed state	July 2008
10850702	Randomised, single-dose, 4-treatment, 4-period, crossover to evaluate the relative bioavailability of Lozanoc® (SUBACAP™) at a dose of 50 mg and Sporanox® at a dose of 100 mg and 200 mg in a fasted state	October 2008
CM3007	Randomised, open-label, four-way crossover - Fed and fasted. To determine bioavailability by comparing 110 mg of Lozanoc® (SUBACAP™) with 200 mg of Sporanox®. In fed and fasted state.	September 2007
<b>Pharmacokinetic study</b>		
CM4799	Randomised, crossover – Fasted. To determine pharmacokinetics	October 1999
<b>Efficacy and Safety study</b>		
Clinical study 70850702	Randomised, double-blind, multi-centre study conducted in the USA comparing Lozanoc® with the US reference product over 12 weeks of treatment. To compare the efficacy and safety of Lozanoc (SUBACAP™) itraconazole (test) and Sporanox itraconazole 100mg capsules (reference) in the treatment of toenail onychomycosis.	

Source: Summary of the bioavailability and pharmacokinetics studies (pg 28 of the submission – Appendix1)

6.4 The details of the bioavailability studies were presented in Appendix 1 of the re-submission. The submission's main observations from these studies were:

- Although the rate and degree of exposure is comparable, itraconazole 50 mg capsules (test) is not bioequivalent to with itraconazole 100 mg (reference) capsules due to the variability of C<sub>max</sub> between the reference and test products. Therefore, the submission stated that instead of showing bioequivalence, a real difference in bioavailability was shown.
- Inter- and intra-patient variability in itraconazole exposure significantly lower with itraconazole 50 mg compared to itraconazole 100 mg.
- Significantly less variation in exposure in a fasted and fed state (high-fat breakfasts) between itraconazole 50 mg and itraconazole 100 mg capsules.

6.5 The minor submission presented comments from two Australian experts (Dr David Ellis and A/Professor Debbie Marriot) on the clinical use and place of itraconazole in the treatment paradigm during the TGA appeal.

### Comparative effectiveness

6.6 The primary outcome from the Study 70850702 was based on superficial mycoses. The submission claimed that itraconazole 50 mg proved to be superior to placebo for each of the three primary endpoints at week 24. Itraconazole 100mg was superior to

placebo at week 24 for the mycological cure parameter but not for the clinical and therapeutic cure parameters.

**Table 2: Results of Study 70850702 – analysis of study endpoints at week 24**

Study arm	Sample	Primary endpoint - Week 24					
		Superiority against placebo			Non-inferiority Test vs. Ref		
	Recruited/ Completed	Therapeutic cure (%)	Clinical cure (%)	Mycological cure (%)	Therapeutic cure (%)	Clinical cure (%)	Mycological cure (Difference Lower 95% CI)
		p-value	p-value	p-value	p-value	p-value	
Test: 100 mg po qd (Lozanoc® 50 mg)	76/76	8 -10.53 p=0.0135*	12 -15.79 p=0.0009*	25 -32.89 p=0.0001*	6.47	10.38	3.17
Ref: 200 mg po qd (Sporanox®)	75/74	3 -4.05 p=0.2861	4 -5.41 p=0.1570	22 -29.73 p=0.0003*	-1.77	0.92	-10.62
placebo	24/24	0 0	0 0	1 -4.17			

Source: Table 6 (p19) of the re-submission

6.7 As this was a minor submission, the results have not been independently evaluated.

*For more details on PBAC's view, see section 7 "PBAC outcome".*

### Comparative harms

6.8 The key adverse events (AEs) from the Study 70850702 are summarised below.

**Table 3: Summary of adverse event reported during Study 70850702**

	Lozanoc® N=76	Sporanox® N=75	Placebo N=24	Total N=175
Number of patients suffering any adverse effect (n, % total patients)	42 (24%)	35 (20%)	13 (7%)	90 (51%)

Source, pg.20 of the submission

6.9 The submission maintained that no significant differences were found between the study product and the reference product in terms of the type, frequency or severity of adverse effects reported or observed during the study. The safety profile of itraconazole 50 mg hard capsules at a dose of 100 mg once daily for 12 weeks was consistent with the known safety profile of itraconazole 100 mg capsules at a dose of 200 mg once daily. No significant differences in the frequency of AEs were observed between the study groups (itraconazole 50 mg, itraconazole 100 mg and placebo).

6.10 As this was a minor submission, the results have not been independently evaluated.

*For more details on PBAC's view, see section 7 "PBAC outcome".*

### **Clinical claim**

- 6.11 The submission claimed non-inferiority to itraconazole 100 mg at a dose of 200 mg daily for the treatment of moderate to severe onychomycosis of the toenail for the three primary endpoints at week 24 and superior to placebo for each of the three primary endpoints at week 24.
- 6.12 The submission states that ‘the only clinical study available is in superficial mycoses and not systemic mycoses’ (pg 18 of the re-submission) and ...and in order for an orally administered drug to be effective for a superficial infection there must be systemic absorption at least equivalent to itraconazole 100 mg, thus further supporting the therapeutic equivalence statement’ (pg 22 of the re-submission).

*For more details on PBAC’s view, see section 7 “PBAC outcome”.*

### **Economic analysis**

- 6.13 No economic comparison was presented. In the spreadsheet with the submission, the sponsor requested an equivalent pack price to itraconazole 100 mg.

### **Quality Use of medicines**

- 6.14 The re-submission stated the negligible risk of prescriber or patient confusion was mitigated by Product Information, and proposed administrative advice in the PBS restrictions. The re-submission claimed that itraconazole 50mg has been available in Australia (private market) and in Spain without any patient or prescriber confusion. The submission does not present any evidence to support this claim.

### **Estimated PBS usage & financial implications**

- 6.15 The re-submission claimed that itraconazole 50 mg will only be taking market share from the established itraconazole market and thus will not be increasing the market further than the growth rate calculated based on the 2010-14 data.
- 6.16 Based on the proposed DPMQ (including a ■% price reduction to the ex-manufactures price in both products), the re-submission estimated a net save to the PBS of less than \$10 million in Year 5 of listing, with a total net save to the PBS of less than \$10 million over the first 5 years of listing. This save would be due to the more uptake of the itraconazole 50mg capsules compared to the itraconazole 100mg capsules. This is summarised in the table below.

**Table 4: Estimated use and financial implication**

Net cost of drug to the PBS/RPBS	Year 1	Year 2	Year 3	Year 4	Year 5
Total net cost to the PBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Total net cost to the RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
Total net cost to Medicare Australia	\$0	\$0	\$0	\$0	\$0
Total net cost to MBS	\$0	\$0	\$0	\$0	\$0
<b>Overall Net Cost to PBS/RPBS</b>					
Overall Net Cost to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]

Source: Summary Sheet, LOZANOC Pbac-minor-submissions\_Aug2015.xlsx

- 6.17 As this was a minor submission, the estimates have not been independently evaluated.

*For more details on PBAC's view, see section 7 "PBAC outcome".*

## **7 PBAC Outcome**

- 7.1 The PBAC recommended the Authority Required (Streamlined) listing of itraconazole 50mg capsule for the same indications (systemic aspergillosis, systemic sporotrichosis, systemic histoplasmosis, disseminated pulmonary histoplasmosis infection, chronic pulmonary histoplasmosis infection, oropharyngeal candidiasis, and oesophageal candidiasis) and with same restriction rules as they currently apply to the PBS-listed itraconazole 100mg capsule.
- 7.2 The PBAC noted that the submission partially addressed the issues raised by the Committee from previous submission considered at the November 2014 meeting.
- 7.3 The PBAC agreed that the nominated comparator itraconazole 100mg capsule was reasonable.
- 7.4 The PBAC noted that the clinical trial presented was not powered to demonstrate bio-equivalence. The PBAC also noted that although the sponsor's claim of higher bioavailability was true for itraconazole 50 mg, the PBAC considered that the Cmax and area under the curve were numerically lower compared with the comparator because the 50 mg dose is less than 100 mg.
- 7.5 The PBAC accepted the submission's claim of lower inter- and intra-patient variability with itraconazole 50mg compared to itraconazole 100mg and claim of therapeutic equivalence.
- 7.6 The PBAC noted that although the clinical efficacy and safety trials were based on superficial mycoses, the TGA accepted extrapolation of evidence for the two indications: superficial mycoses and systemic mycoses.
- 7.7 In making this recommendation, the PBAC noted the sponsor's offer of [REDACTED]% price reduction of itraconazole 50mg capsule compared to the existing PBS-listed

itraconazole 100mg capsule. The PBAC was of the view that an equivalent cost per treatment course should apply to both products, as both are expected to deliver the same clinical outcomes.

- 7.8 The PBAC considered that there may be potential risk of leakage to superficial mycoses and mould prophylaxis and advised to include an administrative note in the restriction that it is not for use in superficial mycoses. The PBAC advised prescriber education/awareness through National Prescribing Service to mitigate the risk of prescriber confusion between the 50mg and 100mg capsules.
- 7.9 In accordance with subsection 101(3BA) of the *National Health Act 1953*, the PBAC advised that itraconazole 50mg capsule should not be treated as interchangeable on an individual patient basis with any other drug.
- 7.10 The PBAC advised that itraconazole 50mg is suitable for prescribing by nurse practitioners within a shared care model, as per the current PBS listing for itraconazole 100mg.
- 7.11 The PBAC recommended that the Safety Net 20 Day rule should not apply as it currently does not apply to itraconazole 100 mg capsule.

**Outcome:**

Recommended

**8 Recommended listing**

Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts		Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5		Lozanoc®	Mayne Pharma

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<b>Condition:</b>	Systemic aspergillosis
<b>PBS Indication:</b>	Systemic aspergillosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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ITRACONAZOLE Capsule, 50mg, 60	1	5		Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Systemic sporotrichosis
<b>PBS Indication:</b>	Systemic sporotrichosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Systemic histoplasmosis
<b>PBS Indication:</b>	Systemic histoplasmosis
<b>Restriction Level / Method:</b>	<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
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Disseminated pulmonary histoplasmosis infection
<b>PBS Indication:</b>	Disseminated pulmonary histoplasmosis infection
<b>Treatment phase:</b>	Treatment and maintenance therapy
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	Patients <i>must be diagnosed with acquired immunodeficiency syndrome (AIDS).</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Chronic pulmonary histoplasmosis infection
<b>PBS Indication:</b>	Chronic pulmonary histoplasmosis infection
<b>Treatment phase:</b>	Treatment and maintenance therapy
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	Patients <i>must be diagnosed with acquired immunodeficiency syndrome (AIDS).</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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ITRACONAZOLE Capsule, 50mg, 60	1	5	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Oropharyngeal candidiasis
<b>PBS Indication:</b>	Oropharyngeal candidiasis
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	<i>Patient must be immunosuppressed.</i>
<b>Administrative Advice</b>	<p><i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i></p> <p><i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i></p> <p><i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i></p> <p><i>Not for use in superficial mycoses.</i></p> <p><i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i></p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
ITRACONAZOLE Capsule, 50mg, 60	1	5	Lozanoc®	Mayne Pharma

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Oesophageal candidiasis
<b>PBS Indication:</b>	Oesophageal candidiasis
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	<i>Patient must be immunosuppressed.</i>
<b>Administrative Advice</b>	<i>One capsule of itraconazole 50 mg (Lozanoc) is therapeutically equivalent to one 100 mg capsule of conventional itraconazole (Sporanox).</i>  <i>The recommended dose of Lozanoc is therefore half the recommended dose for Sporanox.</i>  <i>Lozanoc 50 mg capsules and Sporanox 100 mg capsules are not interchangeable.</i>  <i>Not for use in superficial mycoses.</i>  <i>Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</i>

## 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

Mayne Pharma welcomes the PBAC's decision to recommend Lozanoc for use in patients with systemic fungal infections. Mayne Pharma is delighted to have the

opportunity to work with the Department of Health to provide patients and healthcare professionals another option in treating these systemic fungal infections.