

6.20 TICAGRELOR, Tablet 90 mg, Brilinta[®], AstraZeneca Pty Ltd

1 Purpose of Submission

The Category 3 submission requested a change to the restriction level of ticagrelor (Brilinta[®]) for the treatment of acute coronary syndrome (ACS) from Authority Required (STREAMLINED) to Unrestricted Benefit to align with the recent change in restriction level of clopidogrel for the treatment of ACS.

2 Background

Registration status

- 2.1 Ticagrelor was TGA registered on 21 June 2011 for use in combination with aspirin, for the prevention of atherothrombotic events (cardiovascular death, myocardial infarction and stroke) in adult patients with acute coronary syndromes (unstable angina, non-ST elevation Myocardial Infarction or ST elevation Myocardial Infarction) including patients managed medically, and those who are managed with percutaneous coronary intervention or coronary artery by-pass grafting (CABG).

Previous PBAC consideration

- 2.2 In its July 2011 meeting, the PBAC recommended ticagrelor for the treatment of ACS in combination with aspirin on the basis of acceptable cost-effectiveness compared with clopidogrel in combination with aspirin. Ticagrelor was PBS-listed on 1 August 2012.

3 Requested listing

- 3.1 The submission requested the existing listing of ticagrelor to be amended from Authority Required (STREAMLINED) to Unrestricted Benefit to align with the change in restriction level of clopidogrel that was effective on 1 May 2022.
- 3.2 At its December 2021 Intracycle meeting, the PBAC recommended the listing of clopidogrel and clopidogrel with aspirin be changed from Authority Required (STREAMLINED) to Unrestricted Benefit. The PBAC noted clinician feedback received regarding the barriers that the current Authority Required (STREAMLINED) listings present in certain circumstances and how the place in therapy of clopidogrel has evolved over time. The PBAC considered that unrestricted listings for clopidogrel and clopidogrel with aspirin would reduce the burden for prescribers and enable better access for patients in need of antiplatelet therapy.

- 3.3 The submission claimed that unrestricting the listing of ticagrelor would reduce the administrative burden to Services Australia for processing authority prescriptions and would allow prescribers more consultation time with their patients as prescribers do not need to obtain and include an authority code.
- 3.4 The submission further stated that an unrestricted listing of ticagrelor will avoid confusion created by the disparity in restriction levels following the changes to the PBS restriction of clopidogrel, given that switching from clopidogrel to ticagrelor is known to occur. Given the higher adverse events associated with ticagrelor (e.g. increased non-coronary artery bypass grafting bleeding) and potentially lower compliance arising from a twice-daily dosing schedule compared to clopidogrel’s once daily dosing (para 5.14.34, ticagrelor Public Summary Document (PSD), July 2011 PBAC meeting), it is unclear to what extent switching from clopidogrel to ticagrelor occurs in practice.
- 3.5 Ticagrelor is not TGA indicated for use in the absence of aspirin. Unrestricting ticagrelor would remove the clinical criterion “treatment must be in combination with aspirin,” which may result in usage in a population that is sensitive/allergic/contraindicated to aspirin, who would not have otherwise been PBS eligible for ticagrelor. The Pre-PBAC response argued prescribers would be familiar with prescribing ticagrelor as ticagrelor has been in the Australian market for over 10 years, however, acknowledged the concerns that an unrestricted listing would result in usage in a population that may be sensitive/allergic/contraindicated to aspirin because of the removal of the clinical criterion “treatment must be in combination with aspirin”. The Pre-PBAC response therefore proposed that the restriction level of ticagrelor be changed from Authority Required (STREAMLINED) to a Restricted Benefit. The proposed requested PBS listing for ticagrelor has been updated in the table below.
- 3.6 Suggested additions are in italics and deletions are in strikethrough.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TICAGRELOR					
ticagrelor 90 mg tablet, 56	1418P	1	56	5	Brilinta
Restriction Summary 5746 / Treatment of Concept: 5746					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	Restriction type: <input checked="" type="checkbox"/> <i>Restricted Benefit</i> <input checked="" type="checkbox"/> Unrestricted benefit <input checked="" type="checkbox"/> Authority Required (Streamlined)				
	Clinical criteria: The treatment must be in combination with aspirin				
	Administrative Advice: Shared Care Model: <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>				

Comparator

- 3.6 The submission nominated ticagrelor as the only comparator. This was not appropriate as clopidogrel is a relevant comparator.
- 3.7 In its July 2011 meeting, the PBAC noted clopidogrel as the appropriate main comparator to ticagrelor. The PBAC considered that the results of the head-to-head randomised trial (PLATO) presented in the submission supported the claim of the superior comparative effectiveness of ticagrelor over clopidogrel (para 5.14.29, ticagrelor PSD, July 2011). The PBAC considered the submission's claim of non-inferior safety to clopidogrel was unreasonable (para 5.14.21, ticagrelor PSD, July 2011), noting that it lacked long term safety data beyond 12 months and FDA reports of discontinuations because of dyspnoea and ventricular pauses.

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

4 Financial implications

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

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

Drug cost

- 4.3 At 1 January 2023, the AEMP of ticagrelor was \$114.52 and the DPMQ was \$136.43.

Estimated PBS usage and financial implications

- 4.4 The submission assumed that there will be no increase in the uptake of ticagrelor due to the change in restriction and therefore no financial impact, stating that it has been PBS-listed for 10 years and prescribers are familiar with the drug. As such, the submission did not provide any financial estimates. Clopidogrel is unrestricted on the PBS and is used for ACS and non-ACS indications. As ticagrelor is significantly more expensive than clopidogrel, any substitution of clopidogrel with ticagrelor for non-ACS indications will result in a cost to the Commonwealth. The Pre-PBAC response argued that removing the ACS indication from the restriction would not result in the PBS prescribing of ticagrelor for non-ACS indications and provided financial estimates of the projected growth of ticagrelor for the ACS indication. The PBAC considered that, given there is a risk that ticagrelor may be used for non-ACS indications if unrestricted, the submission's claim of nil financial impact was unreasonable and that the financial estimates should reflect the likely displacement of clopidogrel.
- 4.5 In its July 2011 PBAC meeting, the PBAC considered that the high potential for ticagrelor to be prescribed for non-ACS conditions was of particular concern as use in such conditions has the potential to result in high costs to the PBS. Despite the

consequent uncertainty in the estimated utilisation, the PBAC had considered that the utilisation may be less than estimated due to adverse events associated with ticagrelor (e.g. increased non-CABG bleeding) and potentially lower compliance arising from twice daily dosing compared to clopidogrel’s once daily dosing. Nonetheless, the PBAC noted the sponsor’s willingness to enter into a risk share agreement, to address the issue of ticagrelor’s potential use outside any PBS restriction. The PBAC therefore recommended that the Department enter into a price-volume risk share agreement with the sponsor (para 5.14.34, ticagrelor PSD, July 2011 PBAC meeting). Ticagrelor was previously subject to a Deed of Agreement with a Risk Sharing Arrangement encompassing subsidisation caps, however, the Deed was terminated in 2017 following the end of the nominal Deed Term. The subsidisation caps over the term of Deed were not exceeded.

Table 1: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of PBS/RPBS scripts dispensed ^a	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Estimated financial implications of ticagrelor						
Cost to PBS/RPBS less co-payment	■ ²	■ ³	■ ³	■ ³	■ ³	■ ³
Changed listing	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴	■ ⁴
Net financial implications						
Net cost to PBS/RPBS	■ ⁵	■ ⁵	■ ⁵	■ ⁵	■ ⁵	■ ⁵

^a Assuming 12 per patient per year as estimated by the submission.

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Source: submission financial workbook

The redacted values correspond to the following ranges:

¹ 200,000 to < 300,000

² \$20 million to < \$30 million

³ \$30 million to < \$40 million

⁴ net cost saving

⁵ \$0 to < \$10 million

Committee-In-Confidence information

[Redacted content]

End Committee-In-Confidence information

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

5 PBAC Outcome

5.1 The PBAC did not recommend a change to the restriction level of ticagrelor (Brilinta®) for the treatment of acute coronary syndrome (ACS) from Authority Required (STREAMLINED) to Unrestricted Benefit (as per submission’s initial request) or

Restricted Benefit (as proposed in the Pre-PBAC response) to align with the recent change in restriction level of clopidogrel for the treatment of ACS.

- 5.2 The PBAC considered that the submission's assumption of no increase in the uptake of ticagrelor and no financial impact was unreasonable. The PBAC noted prescribers' familiarity with prescribing ticagrelor and its established place in therapy in practice, however, considered that this did not preclude potential substitution for clopidogrel. Given the disparity in price between clopidogrel and ticagrelor, the PBAC noted that any increase in the uptake of ticagrelor over clopidogrel would result in a cost to the Commonwealth.
- 5.3 The PBAC noted that the submission claimed unrestricting ticagrelor would avoid confusion created by the disparity in restriction levels following the changes to the PBS restriction of clopidogrel. The PBAC disagreed with the submission's claim and considered that prescribers are familiar with prescribing ticagrelor and that the difference in restriction level to clopidogrel is not a cause for confusion. The PBAC noted ticagrelor has an established place in therapy and in practice. The PBAC further noted that the submission did not claim any other additional clinical benefits from unrestricting ticagrelor and considered that there was no scenario in which the lowering of the restriction level would improve patient outcomes.
- 5.4 The PBAC considered that the submission nominated comparator, ticagrelor, was inappropriate and that clopidogrel was the only relevant comparator. The PBAC recalled that, in its July 2011 meeting, it considered clopidogrel as the appropriate main comparator as clopidogrel had the majority of use in clinical practice and shared the same restriction as that which was requested for ticagrelor.
- 5.5 The PBAC suggested any resubmission requesting a restricted benefit for ticagrelor should be presented on a cost-minimisation basis to clopidogrel. A resubmission may be lodged at any future due date for PBAC submissions using the standard re-entry pathway.
- 5.6 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:

Not recommended

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available

through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

The sponsor had no comment.