

6.10 DIMETHYL FUMARATE Capsules (modified release), 120 mg, Tecfidera[®], Biogen Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested an amendment to the PBS maximum quantity of dimethyl fumarate 120 mg capsules to allow flexibility in dose titration for both initial and continuing dose titration periods. No changes are proposed to the existing restriction for continuing therapy for the 240 mg capsules, maximum quantity 56, no of repeats 5.

2 Requested listing

- 2.1 The minor re-submission requested the following new listing.
- 2.2 The submission also sought to remove the grandfather restriction from the continuing treatment phase as this is no longer necessary.
Additions are in italics, deletions in strikethrough.

Initial titration treatment

Name, Restriction, Manner of administration and form	Max. Qty (Packs)	Max. Qty (Units)	No. of Rpts	Proprietary Name and Manufacturer		
Capsules 120 mg	2	28	0	Tecfidera [®]	Biogen	Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Multiple sclerosis
Treatment phase:	Initial <i>titration</i> treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

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Clinical criteria:	<p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by magnetic resonance imaging of the brain and/or spinal cord; OR</p> <p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by accompanying written certification provided by a radiologist that a magnetic resonance imaging scan is contraindicated because of the risk of physical (not psychological) injury to the patient,</p> <p>AND</p> <p>The treatment must be as monotherapy,</p> <p>AND</p> <p>Patient must have experienced at least 2 documented attacks of neurological dysfunction, believed to be due to the multiple sclerosis, in the preceding 2 years,</p> <p>AND</p> <p>Patient must be ambulatory (without assistance or support).</p> <p>Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.</p>
Prescriber Instructions	Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.
Administrative Advice	<p>No increase in the maximum quantity or number of units may be authorised.</p> <p>Note</p> <p>No increase in the maximum number of repeats may be authorised.</p> <p>Note</p> <p>Special Pricing Arrangements apply.</p>

Continuing titration treatment

Name, Restriction, Manner of administration and form	Max. Qty (Packs)	Max. Qty (Units)	No. of Rpts	Proprietary Name and Manufacturer	
Capsules 120 mg	2	28	0	Tecfidera®	Biogen Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Multiple sclerosis
Treatment phase:	Continuing <i>titration</i> treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

Clinical criteria:	<p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by magnetic resonance imaging of the brain and/or spinal cord; OR</p> <p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by accompanying written certification provided by a radiologist that a magnetic resonance imaging scan is contraindicated because of the risk of physical (not psychological) injury to the patient,</p> <p>AND</p> <p>The treatment must be as monotherapy,</p> <p>AND</p> <p>Patient must have previously been issued with an authority prescription for this drug; OR</p> <p>Patient must have been receiving treatment with this drug prior to 1 December 2013,</p> <p>AND</p> <p>Patient must not show continuing progression of disability while on treatment with this drug.</p>
Prescriber Instructions	Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.
Administrative Advice	Note Special Pricing Arrangements apply.

3 Background

- 3.1 Dimethyl fumarate was TGA registered on 11 July 2013 for the treatment of patients with relapsing-remitting multiple sclerosis to reduce the frequency of relapses and to delay the progression of disability.
- 3.2 Dimethyl fumarate has previously been considered by the PBAC twice, in July 2013 and November 2014.
- 3.3 In the submission for the July 2013 PBAC meeting, the sponsor requested listing of the 120 mg strength with three repeats. The PBAC recommended listing of dimethyl fumarate at the July 2013 PBAC meeting. However, it recommended listing the 120 mg strength with zero repeats. The PBAC considered that listing of 120 mg with zero repeats would be more clinically responsible, given that prescribers could still request several repeats for the 120 mg strength if needed.
- 3.4 A risk share arrangement is currently in place for the PBS listing of dimethyl fumarate. The risk share arrangement includes a cap on expenditure for the 120 mg form, with rebates for any expenditure over the cap.
- 3.5 If the listing of dimethyl fumarate is amended, the current risk share arrangements would still apply.

4 Clinical place for the proposed therapy

- 4.1 The submission argued that changing the current listing would streamline processes for continuing on the 120 mg dose for clinicians, Medicare and patients.
- 4.2 To assess the number of patients who received continuing treatment on the 120 mg dose form, the PBAC Secretariat sought from the Drug Utilisation Section, who

advised that ■ patients (■%) received at least one continuing 120 mg script, with no patient receiving more than 3 continuing scripts (see below)

- 4.3 The pre-PBAC response suggested around one-third of all patients receiving dimethyl fumarate will discontinue treatment primarily due to issues with gastrointestinal tolerability and that ■% of patients initiating treatment with dimethyl fumarate requiring a second dispensing of the 120 mg capsule.

Consumer comments

- 4.4 The PBAC noted and welcomed the health care professional (1) input via the Consumer Comments facility on the PBS website. The comment supported making increased maximum quantities available for the dose titration period.

Estimated PBS usage and financial implications

- 4.5 The DUSC Secretariat examined the utilisation of the 120 mg versus 240 mg strength for continuing therapy with dimethyl fumarate in patients initiating on this drug in the 2014-15 financial year. As dimethyl fumarate was first listed on 1 December 2013, it was assumed that grandfathered patients would not be included in the initiating cohort. Data were sourced from the Department of Human Services prescriptions database and the analyses were based on the date of supply. There were ■ initiating patients in 2014-15, of these ■ patients received a continuing supply of dimethyl fumarate with either the 120 mg or 240 mg dose. The analyses were based on the first episode of treatment. If there was a break between supplies of more than 90 days it was assumed that the patient had discontinued treatment.
- 4.6 A low proportion of patients (n=■, ■%) received a first continuation script at the lower dose (120 mg). A summary of the number of continuing prescriptions for the 120 mg strength and the amount of patient contributions paid for these prescriptions is summarised below.

Patient category	N	Median number of continuing supplies of 120 mg	Maximum number of continuing supplies of 120 mg	Mean total patient contribution for continuing supplies of 120 mg	Maximum total patient contribution for continuing supplies of 120 mg
General	■	■	■	\$ ■	\$ ■
Concessional	■	1	■	\$ ■	\$ ■

Source: DHS prescriptions database, accessed on 26 May 2016. Figures are based on the date of supply.

- 4.7 Of the ■ patients who were supplied a continuation script for the higher strength, ■ patients and a subsequent supply at the lower dose.

5 PBAC Outcome

- 5.1 The PBAC recommended increasing the maximum quantities of 120 mg dimethyl fumarate from one to two packs for both the initial and continuing titration periods.
- 5.2 In making its recommendation, the PBAC considered that increasing the maximum quantity of 120 mg DMF may simplify dose titration for both patients and medical practitioners. The PBAC also noted the TGA Product Information allows for downward titration from the 240 mg to the 120 mg dose if necessary.
- 5.3 The PBAC noted the existing Risk Share Arrangement caps Commonwealth expenditure on the 120 mg dose form of dimethyl fumarate, and considered that as expenditure had not approached the cap in any year since listing, the risk of reaching the cap as a result of increased maximum quantities was minimal. As a result, the PBAC was of the opinion that the Risk Sharing Arrangements would not prevent any increase in cost to Government due to the change in maximum quantity. The PBAC advised that the Department should work with the sponsor to determine the likely financial impact of the proposed change over the forward estimates and ensure that it does not have a financial impact for Government.
- 5.4 The PBAC did not accept the request to add the word *titration* to the treatment phase for either the initial or continuing restrictions, as it would be inconsistent with the current approach to the wording of restrictions.
- 5.5 The PBAC agreed the grandfather restriction for the continuing dimethyl fumarate listings should be removed, including for the 240 mg listings not raised in the submission.
- 5.6 The PBAC advised that dimethyl fumarate should remain not suitable for prescribing by nurse practitioners.
- 5.7 The PBAC recommended that the Early Supply Rule should continue to apply.
- 5.8 The PBAC noted that this submission is not eligible for an Independent Review as the proposed changes were recommended.

Outcome:

Recommended

6 Recommended listing

- 6.1 Amend existing listing and maximum quantity as follows and remove grandfathering clause from dimethyl fumarate 240 mg capsule:

Initial titration treatment

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DIMETHYL FUMARATE Capsules 120 mg, 14	2	0	Tecfidera®	Biogen Australia Pty Ltd
Category / Program	GENERAL – General Schedule (Code GE)			
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
Condition:	Multiple sclerosis			
Treatment phase:	Initial treatment			
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined			
Clinical criteria:	<p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by magnetic resonance imaging of the brain and/or spinal cord; OR</p> <p>The condition must be diagnosed as clinically definite relapsing-remitting multiple sclerosis by accompanying written certification provided by a radiologist that a magnetic resonance imaging scan is contraindicated because of the risk of physical (not psychological) injury to the patient,</p> <p>AND</p> <p>The treatment must be as monotherapy,</p> <p>AND</p> <p>Patient must have experienced at least 2 documented attacks of neurological dysfunction, believed to be due to the multiple sclerosis, in the preceding 2 years,</p> <p>AND</p> <p>Patient must be ambulatory (without assistance or support).</p> <p>Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.</p>			
Prescriber Instructions	Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.			
Administrative Advice	No increase in the maximum quantity or number of units may be authorised. Note No increase in the maximum number of repeats may be authorised. Note Special Pricing Arrangements apply.			

Continuing titration treatment

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Condition:	Multiple sclerosis			
Treatment phase:	Continuing treatment			
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required – Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined			
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Prescriber Instructions	Where applicable, the date of the magnetic resonance imaging scan must be provided with the authority application.			
Administrative Advice	Note Special Pricing Arrangements apply.			

7 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.

8 Sponsor's Comment

The sponsor had no comment.