

26 June 2014

Proposal for azacitidine, lenalidomide and thalidomide

PHARMAC is seeking feedback on a provisional agreement with Celgene Pty Ltd. In summary, this proposal is, from 1 September 2014, to:

- Fund azacitidine (Vidaza) 100 mg injection for patients with intermediate-2 or high risk myelodysplastic syndrome (MDS), chronic myelomonocytic leukaemia (CMML) or MDS-associated acute myeloid leukaemia (AML); and
- Fund lenalidomide (Revlimid) 10 and 25 mg capsules for relapsed refractory multiple myeloma (MM); and
- Reduce the price and subsidy for thalidomide (Thalomid) 50 mg and 100mg capsules.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **5pm Thursday, 10 July 2014** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or its delegate) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request.

Details of the proposal

In relation to azacitidine

- Azacitidine (Vidaza) 100 mg vial would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 September 2014. The following price and subsidy would apply (all prices are ex-manufacturer and exclude GST):

Chemical	Presentation	Brand	Pack size	Price/Subsidy
azacitidine	Inj 100 mg vial	Vidaza	1	\$605.00
azacitidine	Inj 1mg for ECP	Baxter	1	\$6.66

- Confidential rebates would apply to Vidaza, reducing its net price to the Funder and/or DHB Hospitals.
- Azacitidine would be listed in Section B of the Pharmaceutical Schedule subject to Special Authority criteria as follows:

Azacitidine – PCT only – Specialist - Special Authority for Subsidy

Initial application — only from a Haematologist or Medical Practitioner on the recommendation of a Haematologist. Approvals valid for 12 months for applications meeting the following criteria:

All of the following

1. Any of the following:
 - 1.1. The patient has International Prognostic Scoring System (IPSS) intermediate-2 or high risk myelodysplastic syndrome; or
 - 1.2. The patient has chronic myelomonocytic leukaemia (10%-29% marrow blasts without myeloproliferative disorder); or
 - 1.3. The patient has acute myeloid leukaemia with 20-30% blasts and multi-lineage dysplasia, according to World Health Organisation Classification (WHO); and
2. The patient has performance status (WHO/ECOG) grade 0-2; and
3. The patient does not have secondary myelodysplastic syndrome resulting from chemical injury or prior treatment with chemotherapy and/or radiation for other diseases; and
4. The patient has an estimated life expectancy of at least 3 months.

Renewal application — only from a Haematologist or Medical Practitioner on the recommendation of a Haematologist. Approvals valid for 12 months for applications meeting the following criteria:

Both:

1. No evidence of disease progression, and
2. The treatment remains appropriate and patient is benefitting from treatment.

- Azacitidine would be listed in Part II of Section H of the Pharmaceutical Schedule subject to a restriction as follows:

Restricted

Haematologist

Re-assessment required after 12 months

Initiation

All of the following:

1. Any of the following:
 - 1.1. The patient has International Prognostic Scoring System (IPSS) intermediate-2 or high risk myelodysplastic syndrome; or

- 1.2. The patient has chronic myelomonocytic leukaemia (10%-29% marrow blasts without myeloproliferative disorder); or
- 1.3. The patient has acute myeloid leukaemia with 20-30% blasts and multi-lineage dysplasia, according to World Health Organisation Classification (WHO); and
2. The patient has performance status (WHO/ECOG) grade 0-2; and
3. The patient does not have secondary myelodysplastic syndrome resulting from chemical injury or prior treatment with chemotherapy and/or radiation for other diseases; and
4. The patient has an estimated life expectancy of at least 3 months.

**Continuation
Haematologist
Re-assessment required after 12 months**

Both

1. No evidence of disease progression, and
2. The treatment remains appropriate and patient is benefitting from treatment.

In relation to lenalidomide

- Lenalidomide (Revlimid) 10 mg and 25 mg capsules would be listed in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 September 2014. The following prices and subsidies would apply (all prices are ex-manufacturer and exclude GST):

Chemical	Presentation	Brand	Pack size	Price/Subsidy
Lenalidomide	Cap 10 mg	Revlimid	21	\$6,207.00
Lenalidomide	Cap 25 mg	Revlimid	21	\$7,627.00

- Confidential rebates would apply to Revlimid, reducing its net price to the Funder and/or DHB Hospitals.
- Lenalidomide would be listed in Section B of the Pharmaceutical Schedule subject to Special Authority criteria as follows:

Lenalidomide –Retail Pharmacy- Specialist - Special Authority for Subsidy
Initial application (Relapsed/refractory disease) — only from a Haematologist or Medical Practitioner on the recommendation of a Haematologist. Approvals valid for 6 months for applications meeting the following criteria:

All of the following:

1. Patient has relapsed or refractory multiple myeloma with progressive disease; and
2. Either:
 - 2.1. The patient has received at least two lines of prior treatment for multiple myeloma including bortezomib and thalidomide; or
 - 2.2. Both:
 - 2.2.1. The patient has received at least one line of prior treatment for multiple myeloma, bortezomib or thalidomide, and
 - 2.2.2. The patient experienced severe (grade ≥ 3), dose limiting, peripheral neuropathy that precludes further treatment with either bortezomib or thalidomide; and

3. Lenalidomide to be administered at a maximum dose of 25 mg/day in combination with dexamethasone.

Renewal application — only from a Haematologist or Medical Practitioner on the recommendation of a Haematologist. Approvals valid for 6 months for applications meeting the following criteria:

Both:

1. No evidence of disease progression, and
2. The treatment remains appropriate and patient is benefitting from treatment.

- Lenalidomide would be listed in Part II of Section H of the Pharmaceutical Schedule subject to a restriction substantially as follows:

**Restricted
Haematologist
Re-assessment required after 6 months
Initiation**

All of the following

1. Patient has relapsed or refractory multiple myeloma with progressive disease; and
2. Either:
 - 2.1. The patient has received at least two lines of prior treatment for multiple myeloma including bortezomib and thalidomide; or
 - 2.2. Both
 - 2.2.1. The patient has received at least one line of prior treatment for multiple myeloma, bortezomib or thalidomide, and
 - 2.2.2. The patient experienced severe (grade ≥ 3), dose limiting, peripheral neuropathy that precludes further treatment with either bortezomib or thalidomide; and
3. Lenalidomide to be administered at a maximum dose of 25 mg/day in combination with dexamethasone.

**Continuation
Haematologist
Re-assessment required after 6 months**

Both:

1. No evidence of disease progression, and
2. The treatment remains appropriate and patient is benefitting from treatment.

In relation to thalidomide (Thalomid):

- The prices and subsidies of thalidomide 50 mg and 100 mg capsules listed in Section B and in Part II of Section H of the Pharmaceutical Schedule would be amended from 1 September 2014 as follows (all prices are ex-manufacturer and exclude GST):

Pharmaceutical	Brand	Pack size	Current price and subsidy	Proposed price and subsidy
Thalidomide cap 50 mg	Thalomid	28	\$504.00	\$420.00
Thalidomide cap 100 mg	Thalomid	28	\$1,008.00	\$840.00

- Thalidomide would remain listed in Section B and Part II of Section H of the Pharmaceutical Schedule subject to Special Authority/Restriction for patients with multiple myeloma or systemic AL amyloidosis.

Background

The Pharmacology and Therapeutics Advisory Committee (PTAC) and the Cancer Treatments Subcommittee of PTAC (CaTSoP) have provided advice on the funding of azacitidine for myelodysplastic syndromes (MDS) and lenalidomide for relapsed refractory multiple myeloma (MM).

In summary PTAC and/or CaTSoP recommended that,

- Azacitidine should be funded for the treatment of patients with intermediate-2 or high risk MDS, CMML or MDS-associated AML with low priority;
- Lenalidomide should be funded as a second line treatment option for multiple myeloma patients who have experienced significant, persistent, intractable peripheral neuropathy following treatment with bortezomib or thalidomide with medium priority; and
- Lenalidomide should be funded as a third line treatment for multiple myeloma after prior treatment with bortezomib and thalidomide with low priority.

Azacitidine minutes can be found here:

<http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=358>

Lenalidomide minutes can be found here:

<http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=288>

<http://www.pharmac.govt.nz/patients/ApplicationTracker?ProposalId=1196>

Thalidomide is currently listed on the Pharmaceutical Schedule, under Special Authority criteria for treatment of multiple myeloma or systemic AL amyloidosis. Current expenditure on thalidomide is approximately \$2 million per annum.

Myelodysplastic syndromes (MDS)

The term MDS encompasses a variety of closely related blood conditions characterised by chronic cytopenias (anemia, neutropenia, thrombocytopenia) accompanied by abnormal cellular maturation. MDS occurs most commonly in older adults with the risk of developing MDS increasing with age. Patients with MDS are at risk for symptomatic anemia, infection, and bleeding, as well as progression to acute myeloid leukemia (AML). MDS is an incurable disease, the main goal of treatment is to control symptoms, improve quality and length of life, and to decrease the risk of progression to AML.

Currently, New Zealand MDS patients requiring treatment receive either high dose chemotherapy, low-dose cytarabine, or best supportive care such as red blood cell and platelet transfusions, antibiotic treatment (prophylaxis and/or treatment), growth factor support (including GCSF and erythropoietin), and iron chelation. There is a high unmet health need for effective and curative MDS treatments. Currently funded treatments, including chemotherapy, and the proposed treatment, azacitidine, are not curative.

Azacitidine

Azacitidine is a chemical analogue of cytidine, a nucleoside present in DNA and RNA. Clinical trial evidence demonstrates that azacitidine treatment increases overall survival in patients with MDS by approximately 9 months compared with conventional care (best

supportive care low-dose cytarabine, or high dose chemotherapy). In the same trial azacitidine also reduce the number of transfusions required, and total units administered, in patients per annum compared with conventional care.

It is anticipated that, if funded as proposed, up to 200 patients per year would access funded azacitidine.

Multiple Myeloma (MM)

MM is a cancer of plasma cells, a type of white blood cell normally responsible for the production of antibodies. Collections of abnormal cells accumulate in bones, where they cause bone lesions, and in the bone marrow where they interfere with the production of normal blood cells. Multiple Myeloma predominantly affects older individuals. MM is an incurable disease, the main goal of treatment is to control symptoms and to improve quality and length of life.

Currently funded treatment options for New Zealand MM patients include thalidomide, bortezomib, high dose dexamethasone, melphalan and/or induction chemotherapy followed by a stem cell transplant. Both bortezomib and thalidomide treatment are associated with treatment limiting peripheral neuropathy. Treatment options for patients whose disease has relapsed following prior treatment with thalidomide and bortezomib are limited to include retreatment with thalidomide or high dose dexamethasone.

There is a high unmet health need for effective and curative MM treatments. Currently funded treatments, including bortezomib and thalidomide, and the proposed treatment, lenalidomide are not curative.

Lenalidomide

Lenalidomide is an analogue of thalidomide. Lenalidomide has multiple mechanisms of action including immunomodulatory, anti-neoplastic, anti-angiogenic and pro-erythropoietic properties. Like thalidomide, if lenalidomide is taken during pregnancy it may cause birth defects or death to an unborn baby therefore it is contraindicated in women who are pregnant and should be used with caution in females of child bearing potential.

Lenalidomide has a lower rate of peripheral neuropathy compared with bortezomib and thalidomide, so it may be a useful treatment option in patients with relapsed refractory disease who experience treatment limiting peripheral neuropathy with first line bortezomib or thalidomide.

Clinical trial evidence demonstrates that lenalidomide increases survival by approximately 4 months compared with dexamethasone in patients with relapsed refractory MM. There are no head to head trials comparing lenalidomide with thalidomide or bortezomib in relapsed refractory MM.

It is anticipated that, if funded as proposed, up to 170 patients per year would access funded lenalidomide.