

22 March 2010

Proposal to widen funded access to octreotide for patients with malignant bowel obstruction or acromegaly

PHARMAC is seeking feedback on a proposal to widen funded access to octreotide. In summary, the proposal involves widening access to subsidised octreotide to include funding for:

- The treatment of nausea and vomiting in patients with malignant bowel obstruction where treatment with antiemetics, rehydration, antimuscarinic agents, corticosteroids and analgesics has failed; and
- The treatment of acromegaly in patients unwilling or unable to undergo surgery and where radiotherapy is contraindicated or for an interim period until radiotherapy becomes fully effective.

We also propose minor amendments to the current initial and renewal Special Authority criteria for patients with acromegaly where treatment with surgery, radiotherapy, bromocriptine and other oral treatments has failed.

Octreotide is not currently registered by Medsafe for the treatment of nausea and vomiting in patients with malignant bowel obstruction. As such, this part of the proposal is for an off-label indication and, therefore, clinicians would need to comply with Section 25 of the Medicines Act to prescribe octreotide for this use.

More details of the proposal, including the proposed changes to the Special Authority criteria, can be found on the following pages.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback please submit it in writing by 4 pm on **Thursday, 8 April 2010** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or Chief Executive acting under delegated authority) prior to making a decision on this proposal.

Details of the proposal

From 1 July 2010 the Special Authority criteria applying to octreotide (injection 50 µg per ml, 1 ml, 100 µg per ml, 1 ml and 500 µg per ml, 1 ml; LAR 10 mg prefilled syringe, LAR 20 mg prefilled syringe and LAR 30 mg prefilled syringe) would be amended as follows (additions in bold, deletions in strikethrough):

Special Authority for Subsidy

Initial application – (Malignant Bowel Obstruction) from any relevant practitioner. Approvals valid for 1 month for applications meeting the following criteria:

All of the following:

- 1 The patient has nausea* and vomiting* due to malignant bowel obstruction*; and**
- 2 Treatment with antiemetics, rehydration, antimuscarinic agents, corticosteroids and analgesics for at least five days has failed; and**
- 3 Octreotide to be given up to a maximum dose of 1,500 µg daily for up to 3 weeks.**

Renewal – (Malignant Bowel Obstruction) from any relevant practitioner. Approvals valid for 3 months where the treatment remains appropriate and the patient is benefiting from treatment.

Note: indications marked with * are Unapproved Indications.

Initial application – (Acromegaly) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 3 months for applications meeting the following criteria:

Both:

- 1 The patient has acromegaly; and**
- 2 Any of the following**
 - 2.1 Treatment with surgery, radiotherapy and a dopamine agonist has failed; or**
 - 2.2 Treatment with octreotide is for an interim period while awaiting the effects of radiotherapy and a dopamine agonist has failed; or**
 - 2.3 The patient is unwilling, or unable, to undergo surgery and radiotherapy is contraindicated.**

Renewal – (Acromegaly) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 2 years for applications meeting the following criteria:

1 Both:

- 1.1 IGF1 levels have decreased since starting octreotide; and**
- 1.2 The treatment remains appropriate and the patient is benefiting from treatment.**

Note: In patients with acromegaly octreotide treatment should be discontinued if IGF1 levels have not decreased after 3 months treatment. In patients treated with radiotherapy octreotide treatment should be withdrawn every 2 years, for 1 month, for assessment of remission. Octreotide treatment should be stopped where there is biochemical evidence of remission (normal IGF1 levels) following octreotide treatment withdrawal for at least 4 weeks.

Initial application – (Other Indications) only from a relevant specialist or medical practitioner on the recommendation of a relevant specialist. Approvals valid for 2 years for applications meeting the following criteria:

Any of the following:

~~1 Both:~~

- ~~1.1 Acromegaly; and~~
- ~~1.2 Patient has failed surgery, radiotherapy, bromocriptine and other oral therapies; or~~

- 21 VIPomas and Glucagonomas - for patients who are seriously ill in order to improve their clinical state prior to definitive surgery; or
- 32 Both:
 - 32.1 Gastrinoma; and
 - 32.2 Either:
 - 32.2.1 Patient has failed surgery; or
 - 32.2.2 Patient in metastatic disease after H2 antagonists (or proton pump inhibitors) have failed; or
- 43 Both:
 - 43.1 Insulinomas; and
 - 43.2 Surgery is contraindicated or has failed; or
- 54 For pre-operative control of hypoglycaemia and for maintenance therapy; or
- 65 Both:
 - 65.1 Carcinoid syndrome (diagnosed by tissue pathology and/or urinary 5HIAA analysis); and
 - 65.2 Disabling symptoms not controlled by maximal medical therapy.

Note: The use of octreotide in patients with fistulae, oesophageal varices, miscellaneous diarrhoea and hypotension will not be funded as a Special Authority item.

Renewal – **(Other Indications)** only from a relevant specialist **or medical practitioner on the recommendation of a relevant specialist**. Approvals valid for 2 years where the treatment remains appropriate and the patient is benefiting from treatment.

The listed prices of octreotide, and any contractual arrangements with suppliers, would not change under this proposal.

Background to proposal

Octreotide acetate is a synthetic somatostatin analogue. Octreotide is available as an immediate release subcutaneous injection administered 2-3 times daily or a long-acting (LAR) depot intramuscular injection administered once every 4 weeks.

Malignant Bowel Obstruction

Malignant bowel obstruction is a complication in patients with advanced abdominal or pelvic cancer. Surgery to remove, or bypass, the obstruction may be considered; however, many of these patients are terminally ill and unfit for surgery. Medications such as antiemetics, anti-muscarinics, corticosteroids and pain relief are generally considered as the first treatment options for the symptomatic management of nausea and vomiting in these patients. However, some patients do not receive an adequate response to these treatments, in which case the placement of a nasogastric tube (NGT), palliative venting gastrostomy (PVG) or sedation (no treatment) may be used. The quality of life in these terminally ill patients is very poor and their life expectancy is short, typically less than two weeks.

The Analgesic Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC) recommended, with a high priority, that funded access to octreotide be widened to include management of nausea and vomiting in patients with malignant bowel obstruction unresponsive to first-line treatment with anti-muscarinic agents, steroids and antiemetics.

PTAC considers that there is a high level of unmet clinical need in these patients, in whom prognosis is very poor. Having reviewed evidence from a number of studies, PTAC considered that octreotide may be effective at reducing the symptoms of malignant bowel obstruction (nausea, vomiting, secretions and pain) in some patients who have not responded to antimuscarinics. PTAC recommended that the Special Authority for octreotide should be widened and gave this recommendation a high priority.

Acromegaly

Acromegaly is a disease characterised by increased and unregulated growth hormone production, usually caused by a somatotroph tumour in the pituitary gland. The condition is rare, with annual incidence estimated to be 3-4 new cases per million population per year.

Growth hormone stimulates the production of insulin-like growth factor I (IGF-1), which is the primary mediator of the growth-promoting effects of growth hormone. Excess growth hormone is associated with a range of symptoms, including acral overgrowth (i.e., macrognathia; enlargement of the facial bone structure; enlarged hands and feet; visceral overgrowth, including macroglossia and enlarged heart muscle, thyroid, liver, kidney), insulin antagonism, nitrogen retention, and increased risk of colon polyps and tumours. Mortality in patients with acromegaly is at least twice that of the general population with an average life expectancy of 10 years less than the general population.

Current treatment for patients include surgical resection of the tumour, radiotherapy and pharmaceutical treatment both to decrease growth hormone and IGF-1 concentrations and also treat the symptoms of disease. Pharmaceutical treatments include somatostatin analogues (e.g. octreotide) and dopamine agonists (e.g. bromocriptine), which bind directly to specific tumour receptors and inhibit growth hormone secretion.

PHARMAC received applications from clinicians for funding of octreotide to be widened to include pre-surgical treatment of acromegaly, treatment of acromegaly in patients unsuitable for surgery and/or where surgery was not curative and/or where radiotherapy was administered but its effect not yet apparent.

Currently octreotide is only funded for acromegalic patients where treatment with surgery, radiotherapy, bromocriptine and other therapies have failed. PTAC noted that the only relevant oral therapy would be bromocriptine; therefore, the phrase 'and other oral therapies' could be removed from the Special Authority criteria.

PTAC considered that in some studies pre-surgical octreotide treatment was associated with some tumour shrinkage and/or tumour softening, however there was no good evidence that this, rather than other factors such as surgical skill, improved surgical cure rates. PTAC recommended that applications for pre-surgical octreotide treatment of acromegaly be considered on a case by case basis under the Exceptional Circumstances scheme.

PTAC considered that it would be appropriate to amend the Special Authority to be to include acromegalic patients unfit or unwilling to undergo surgery, or in the interim period until radiotherapy becomes fully effective in line with octreotide's registered indication. PTAC considered that amending the Special Authority thus would not result in many additional patients accessing funded treatment since only four EC applications for acromegaly had been received since July 2005.

Full copies of relevant PTAC and Analgesic Subcommittee minutes can be found on the PHARMAC website at:

<http://www.pharmac.govt.nz/2007/11/01/070308.pdf>

<http://www.pharmac.govt.nz/2009/07/15/2009-05%20PTAC%20minutes.pdf>

<http://www.pharmac.govt.nz/2009/07/21/2009-3%20%20Analgesic%20Subcommittee%20Minutes.pdf>