NOTIFICATION

PHARMAC
Pharmaceutical Management Agency

7 August 2013

Approval of proposal to widen access to imiglucerase for type 1 and type 3 Gaucher disease

PHARMAC is pleased to announce the approval of a proposal to widen access to imiglucerase (Cerezyme) from 1 September 2013.

This proposal was the subject of a consultation letter dated 26 June 2013 which can be found on PHARMAC's website at: http://www.pharmac.health.nz/news/item/proposal-to-widen-access-to-imiglucerase-for-type-1-and-type-3-gaucher-disease

In summary, the effect of the decision is that:

- The access criteria will be widened to included funded access to imiglucerase for patients with type 3 Gaucher disease;
- The maximum funded dose of imiglucerase will be increased from 15 iu/kg per month to 30 iu/kg per month for children with type 1 or type 3 Gaucher disease meeting certain criteria.

Details of the decision

Access to imiglucerase (Cerezyme) in Section B of the Pharmaceutical Schedule will be as follows from 1 September 2013:

ELIGIBILITY CRITERIA FOR IMIGLUCERASE

ELIGIBILITY CRITERIA FOR IMIGLUCERASE FUNDING
These guidelines are intended to assist relevant practitioners in gauging which patients are likely to be approved for imiglucerase. In view of the complexity of Gaucher disease severity assessment, each application is thoroughly evaluated by the Gaucher Panel to determine the appropriate imiglucerase treatment.

All requested studies should be carried out in line with the relevant professional guidelines. Patients with Gaucher disease who meet the following criteria may be eligible for initiation of imiglucerase treatment based on current clinical evidence.

Patients eligible for initial approval of Special Authority

1. The patient must have a diagnosis of symptomatic type 1 or type 3 Gaucher disease by the demonstration of:

    - Specific deficiency of glucocerebrosidase in leukocytes or cultured skin fibroblasts; and
    - Genotypic analysis

    Histology and genotype tests to be supplied with the initial application once available. Baseline MRI whole body Short Tau Inversion Recovery (STIR) and serum chitotriosidase reports must be provided.

2. Patients who have Gaucher type 2 disease are not eligible for subsidised treatment. If a patient has a medical condition which significantly impacts on life expectancy or the treatment would not have a significant chance of causing an improvement in the patient's condition, it is considered inappropriate to initiate therapy with imiglucerase.

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3. Patients who receive government funded imiglucerase treatment must be willing to participate in the long term evaluation of the efficacy of the treatment, as approved, if necessary, by an ethics committee. Collated data collected may be made available to international investigators. Patient anonymity should be preserved.

4. Consent for data collection must be obtained from the patient and his/her legal guardian(s), where appropriate in line with any ethics committee process and/or procedural requirements.

5. Unless otherwise agreed by PHARMAC, imiglucerase shall not be subsidised at a dose exceeding 30 iu/kg/month rounded to the nearest whole vial.

6. The Gaucher Panel will consider applications and provide advice on the appropriate management of any other patients referred to it by PHARMAC.

Initial Treatment criteria

Imiglucerase 15 iu/kg/month
One of the following clinical parameters would be severe enough to cause symptoms and as such are considered sufficient to warrant therapy with imiglucerase 15 iu/kg/month.

Imiglucerase 30 iu/kg/month for children*
Any three of the following clinical parameters, or bone crisis, or severe/significant bone marrow abnormalities on MRI would indicate severe disease and warrant initial therapy with imiglucerase 30 iu/kg/month. Unless there are exceptional circumstances only children are eligible for a starting dose of 30 iu/kg/month.

Haematological complications:

1. Haemoglobin <95g/l, after other causes of anaemia, such as iron deficiency have been treated or ruled out, or severe symptoms from anaemia at a higher level of haemoglobin.
2. Thrombocytopenia < 50 x 10E9/L on two separate occasions at least one month apart.
3. Bleeding complications associated with thrombocytopaenia, irrespective of the platelet count.
4. At least two episodes of severely symptomatic splenic infarcts confirmed by CT or other imaging of the abdomen.
5. Massive symptomatic splenomegaly.

Skeletal complications:

1. One acute bone crisis severe enough to require hospitalisation and or major pain management strategies.
2. Radiographical MRI evidence of incipient destruction of any major joint, such as the hips or shoulder.
3. Spontaneous fractures or vertebral collapse.
4. Chronic bone pain not controlled by the administration of non-narcotic analgesics or anti-inflammatory drugs, or requiring continuous medication or causing a significant loss of time from work or school.

Hepatic complications:

1. Evidence of significant liver dysfunction, such as incipient portal hypertension, attributable to Gaucher disease (treatment should start before this stage is reached).
2. Significant hepatomegaly e.g., >2.5 times the normal liver volume or significant abnormality of the liver function tests.

Pulmonary complications:

Reduced vital capacity from clinically significant or progressive pulmonary disease due to Gaucher disease.

Systemic complications:

Growth failure in children: significant decrease in percentile linear growth over a 6-12 month period.

Test reports, including MRI whole body STIR, serum chitotriosidase and haematological data, must accompany the initial application.

'Children' can be defined by an upper age of 18 or the attainment of radiological evidence of skeletal maturity (whichever is the latter).

Patients eligible for renewal of Special Authority

Renewal applications must be submitted to the Gaucher Panel for an annual review.

Renewal of imiglucerase treatment - 15/iu/kg/month

a) If the patient has demonstrated a symptomatic improvement or no deterioration in the main symptom for which therapy was initiated as set out below:
    - bleeding abnormalities;
    - chronic fatigue;
    - gastro intestinal complaints;
    - bone pain; or
    - psychosocial function,

   combined with clinically objective improvement or no deterioration in haemoglobin levels, platelet counts and liver and spleen size, then treatment should be continued.

Renewal of imiglucerase treatment - 30/iu/kg/month:

Success of imiglucerase treatment at 30 iu/kg/month will be based on improvements, or no deterioration in the symptoms for which treatment was initiated.

Primary success measures

a) Radiological (MRI) signs of bone activity performed one year and then two years after treatment begins. At two years there needs to be no deterioration shown by the MRI, compared with MRI taken immediately prior to commencement of therapy increased dose; and

b) serum chitotriosidase levels show a decrease (preferably of 10%) compared with level taken immediately prior to commencement of increased dose. Serum chitotriosidase levels during treatment are to be taken at least at 6 month intervals.

a) visceral and haematological indices (haemoglobin levels, platelet counts, bleeding episodes associated with thrombocytopaenia at any level, liver size, liver function tests, spleen size, episodes of splenic infarction, pulmonary vital capacity); and/or

b) frequency and/or severity of acute bone crises, radiographic signs of incipient major joint destruction, spontaneous fractures or vertebral collapse; and/or

c) systemic complications (namely growth failure); and/or

d) the main symptom(s) for which therapy was initiated +/- increased bleeding abnormalities; chronic fatigue; gastro intestinal complaints; bone pain (chronic bone pain not controlled by the administration of non-narcotic analgesics or anti-inflammatory drugs, or requiring continuous medication or causing a significant loss of time from work or school); or psychosocial function.

Dose Increase Criteria for children

Eligibility criteria for children who have not responded or show poor improvement on 15 iu/kg/month. Clinicians may apply for an increased dose of up to 30 iu/kg/month, rounded to the nearest whole vial. Test results for the following clinical markers, including a repeat MRI whole body STIR and repeat serum chitotriosidase levels must be provided.

Patients are on standard imiglucerase treatment (15 iu/kg/month) and adhering to treatment, and either:

a) (Earlier stage) objective indications of lack of improvement +/- incipient clinical deterioration:
    (i) MRI signs of persistent ongoing or increased bone activity; and
    (ii) Persistent significantly elevated serum chitotriosidase levels; or

(iii) Failure to demonstrate a decline in serum chitotriosidase levels

and/or:

b) (Later stage) deterioration in other laboratory and radiological measures of visceral, haematological or skeletal deterioration (haemoglobin levels, platelet counts, hepatomegaly, liver function tests, splenomegaly, radiological signs of pathological fracture joint destruction), and/or:

c) (Later stage) frank symptomatic deterioration in main initiating symptoms (bleeding abnormalities; chronic fatigue; gastro intestinal complaints; bone pain, osteonecrotic sequelae, etc.)

The during treatment serum chitotriosidase levels are to be taken at least 6 monthly, and an MRI performed at 12 and 24 months after beginning new treatment dose.

Dose stopping criteria for all patients

a) In the event that the Panel determines by some measurable method (for example of a patient refuses on more than three occasions to have injection, or loses product) that the patient has failed to comply adequately with the treatment or measures to evaluate the effectiveness of the therapy, the Panel is to :

(i) notify PHARMAC of its concerns in respect of that patient; and

(ii) make a recommendation to PHARMAC regarding whether funding of imiglucerase for that patients should be withdrawn, and if not, the period and specific conditions under which the Panel would recommend continuance of funding for treatment.

b) In the event of a severe drug reaction treatment may have to be discontinued.

c) If there has been no significant response to treatment at 15iu/kg/month or 30iu/kg/month after 12 months (visceral or haematological), imiglucerase will be discontinued. (Bony changes may require a longer period of treatment and cases will be assessed on an individual basis by the panel).

Feedback received

We appreciate all of the feedback that we received and acknowledge the time people took to respond. All consultation responses received by 10 July 2013 were considered in their entirety in making a decision on the proposed changes. Most responses were supportive of the proposal, and the following key issue was raised in relation to the proposal:

Theme	PHARMAC comment
A responder expressed concern that there is no justification in principle for not also providing for possible dose increases for adults where this is clinically indicated.	The clinical advice received at this stage recommends a dosage of 30 iu/kg/month only for children unless by exception and this is reflected in the eligibility criteria. The Gaucher Panel previously noted that it is clinically appropriate to reduce the dose at an older age. PHARMAC is able to consider dosage increases for adult patients by exception under the Named Patient Pharmaceutical Assessment process (NPPA).

More information

If you have any questions about this decision, you can call our toll free number (9 am to 5 pm, Monday to Friday) on 0800 66 00 50.