

28 July 2009

## Listing of Low Molecular Weight Heparin in the Pharmaceutical Schedule

PHARMAC is pleased to announce the listing of the Clexane brand of low molecular weight heparin on the Pharmaceutical Schedule from 1 August 2009. In summary, the effect of the decision is that:

- Clexane will be listed in the Community Section of the Pharmaceutical Schedule under Special Authority Criteria (this will result in full funding for patients when Clexane is prescribed by a General Practitioner);
- Clexane will be the only brand of low molecular weight heparin that will be listed in Section B of the Pharmaceutical Schedule until 30 June 2012;
- Clexane will be the only brand of enoxaparin available for purchase by DHB hospitals until 30 June 2012 (subject to Discretionary Variance allowance); and,
- Dalteparin and tinzaparin, in addition to enoxaparin, will still be able to be prescribed in DHB hospitals for use in the community via the Discretionary Community Supply (DCS) mechanism (the DCS criteria will not change).

## Details of the Decision

### Pricing

Clexane will be listed in Sections B and H of the Pharmaceutical Schedule at the following prices and subsidies (ex-manufacturer, exclusive of GST):

<i>Chemical</i>	<i>Brand</i>	<i>Form</i>	<i>Strength</i>	<i>Pack Size</i>	<i>Price and Subsidy</i>
			20 mg	10	\$39.20
			40 mg	10	\$52.30
			60 mg	10	\$78.85
Enoxaparin sodium	Clexane	Injection	80 mg	10	\$105.12
			100 mg	10	\$135.20
			120 mg	10	\$168.00
			150 mg	10	\$192.00

### Funded indications for community access – Section B of the Pharmaceutical Schedule

Clexane will be the only brand of low molecular weight heparin listed in Section B of the Pharmaceutical Schedule until 30 June 2012 (it will have Low Molecular Weight Heparin Sole Supply Status).

Clexane (enoxaparin) will be listed in the Community Section of the Pharmaceutical Schedule (Section B) from 1 August 2009 under the Special Authority Criteria below.

### **Special Authority for Subsidy**

**Initial application - (Pregnancy or Malignancy)** from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

Either:

- 1 Low molecular weight heparin treatment is required during a patients pregnancy; or
- 2 For the treatment of venous thromboembolism where the patient has a malignancy.

**Initial application - (Venous thromboembolism other than in pregnancy or malignancy)** from any relevant practitioner. Approvals valid for 1 month for applications meeting the following criteria:

Any of the following:

- 1 For the short-term treatment of venous thromboembolism prior to establishing a therapeutic INR with oral anti-coagulant treatment; or
- 2 For the prophylaxis and treatment of venous thromboembolism in high risk surgery; or
- 3 To enable cessation/re-establishment of existing warfarin treatment pre/post surgery; or
- 4 For the prophylaxis and treatment of venous thromboembolism in Acute Coronary Syndrome surgical intervention; or
- 5 To be used in association with cardioversion of atrial fibrillation.

**Renewal application - (Pregnancy or Malignancy)** from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:

Either:

- 1 Low molecular weight heparin treatment is required during a patients pregnancy; or
- 2 For the treatment of venous thromboembolism where the patient has a malignancy.

**Renewal application - (Venous thromboembolism other than in pregnancy or malignancy)** from any relevant practitioner. Approvals valid for 1 month for applications where:

- 1 Low molecular weight heparin treatment or prophylaxis is required for a second or subsequent event (surgery, ACS, cardioversion, or prior to oral anti-coagulation).

The Special Authority form is available at  
<http://www.pharmac.govt.nz/2009/08/01/SA0975.pdf>

With respect to the Special Authority:

- It was not possible to replicate the DCS criteria in a Special Authority for a number of reasons, including that part-months are unable to be processed by the Special Authority system. The criteria therefore look different, but cover (at least) the same indications.
- The initial applications are for a set period depending upon the type of event/indication that has occurred. The Special Authority system does not allow for a patient to have two initial applications for the same Special Authority (ie if a patient required enoxaparin for two pregnancies, or require enoxaparin for high risk surgery and then a malignancy). To address this, renewal criteria have been provided so that enoxaparin can be funded for a second event.

## Access through hospitals – Section H of the Pharmaceutical Schedule

Clexane will be the only brand of enoxaparin available for use in DHB hospitals until 30 June 2012 (subject to a Discretionary Variance (DV) limit of 1%).

The current provisions for the use of low molecular weight heparin in DHB hospitals would continue, including the current ability to use:

- other LMWHs such as dalteparin and tinzaparin; and,
- the current Discretionary Community Supply (DCS) criteria for enoxaparin, dalteparin and tinzaparin.

## **Feedback received during consultation**

We appreciated all the feedback that we received from the consultation (dated 29 June 2009) and acknowledge the time that people took to respond. All consultation responses were considered by PHARMAC's Board before it made its decision.

There was significant support for the proposal from a number of the responders, mainly on the following grounds:

- improvement in accessibility;
- opening up opportunities for better management of patients in the community with support from haematology services;
- enhancement of nationwide VTE prevention activities; and,
- it would work well where it is used in long-term treatment (pregnancy and malignancy).

A number of variations to the proposed Special Authority were suggested, and the Special Authority wording has been amended to include a number of these.

A number of issues were raised in the consultation responses. The following table illustrates the main issues and also PHARMAC's response to these concerns:

### **Venous thromboembolism**

#### *Issue Raised in Consultation*

There were a number of concerns raised regarding the appropriateness of general practitioners being able to prescribe funded low molecular weight heparin. These concerns related to the ability for general practitioners to be able to prescribe LMWH safely and effectively. With respect to this it was noted that:

- Treatment in New Zealand is currently of the highest standard in the world and that this is likely to be due to almost all thrombosis patients being seen in a public hospital thrombosis service.
- DHB thrombosis services use evidence based protocols which are consistently applied and that there is not adequate infrastructure in place to support widespread GP prescription of LMWH for venous thromboembolic disease.
- General practitioners may not perform an adequate diagnosis, determine the dose accurately, or educate and transfer patients to warfarin adequately.
- The incidence of major bleeding may increase.
- The incidence of renal impairment and/or renal failure may increase as GPs do not always measure renal function. It was noted that SQM sent an alert in January 2008

regarding the safe use of LMWH in patients with renal impairment.

- GPs may only treat one or two case of acute VTE per year (the annual incidence is from 0.5 to 1 case per 1000 persons per years)

#### *PHARMAC's Response*

With respect to these issues we note that:

- We are not aware of any evidence that supports the contention that providing access to funding for LMWH to non-specialists (General Practice) would lower the existing high quality of care or result in any additional safety risk.
- GPs can already prescribe LMWH (for private purchase), and warfarin (funded) and are therefore already able to treat these patients.
- We agree that experience with LMWH is not likely to be high in general practice, in part due to it not being funded previously, however while a listing on the Community Pharmaceutical Schedule would enable funded LMWH to be prescribed a clinician can still refer patients to other services, or seek additional training or advice, if they lack diagnosis or treatment expertise (we note that it is the prescribers responsibility to ensure they are competent to diagnose and prescribe and that in the event that they are not, it would be their responsibility to refer the patient to another practitioner).
- Not all hospitals have a specialist VTE service, and not all patients have readily available access to a hospital for the purposes of diagnosis or provision of treatment immediately, or for a longer period when required, this is especially relevant in the case of rural patients.
- Funding for warfarin treatment through General Practice is already available and therefore GPs are already transferring patients to warfarin. This proposal would not alter that situation. We also understand that some DHBs are trying to devolve services to primary care and some now have special access to diagnostic procedures in the community for primary care to access.
- The SQM alert which was sent to clinical leaders in Primary Health Organisations was not targeted specifically to general practitioners and this could be re-implemented.
- A "Specialist" requirement would also erode many of the benefits of the proposal.

#### *Issue Raised in Consultation*

It was considered that enoxaparin should be available with no restrictions or by endorsement as it can take 4-5 days for a Special Authority to be approved for clinicians not using the electronic Special Authority system and this is impractical for DVT.

#### *PHARMAC's Response*

Many clinicians, particularly in General Practice, have access to electronic Special Authorities, which provide means for gaining instant authorisation. In addition, continued use of the current DCS mechanism would remain, thus allowing continued use of the current system. Therefore hospitals would still be able to dispense directly to community patients (e.g. for those that present at ED).

#### *Issue Raised in Consultation*

The rationale for the length of the Special Authority approval for DVT (one month) was questioned as there should be major concerns if LMWH is required to be extended beyond 10-14 days in the initiation of warfarin as this suggests that the prescriber is not competent to initiate warfarin.

#### *PHARMAC's Response*

We agree that warfarin should be able to be initiated in patients within 14 days (this is consistent with the current DCS criteria). The one month approval was not based upon the time taken to reach a therapeutic INR. Instead, it was based upon the fact that the Special Authority system requires a time limit, and as there are a number of indications where the length of use of LMWH differs we have attempted to simplify the Special Authority by

pragmatically grouping a number of the indications together. The length of approval for funding is not a recommendation for use.

## **Surgery**

### *Issue Raised in Consultation*

It was suggested that it is unreasonable for an anaesthetist/specialist to apply for a special authority number for a four-day supply of LMWH, and that this step might often be overlooked, thus disadvantaging the patient (presumably as they would have to pay for the medication).

### *PHARMAC's Response*

We are aware that it may be impractical for some situations within the hospital environment for anaesthetists, ED staff, and other clinicians to access Special Authorities in a timely manner. In these cases hospitals would continue to fund LMWH for inpatients and emergency cases as they currently do. In addition the current DCS provisions would also remain for cases where the hospital wishes to fund treatment for community patients directly.

## **Cardioversion of atrial fibrillation**

### *Issue Raised in Consultation*

It was suggested that the use of LMWH for patients being commenced on oral anti-coagulation for atrial fibrillation should be considered.

### *PHARMAC's Response*

We consider that this is covered by the "To be used in association with cardioversion of atrial fibrillation" criteria.

## **Pregnancy**

### *Issue Raised in Consultation*

It was questioned as to whether the pregnancy criteria allowed the use of LMWH 8 weeks post partum as per the current DCS criteria.

It was noted that there are no current guidelines for the treatment and prevention of pregnancy-associated VTE (including dosage and duration) and it would therefore be premature to extend access to LMWH in pregnancy to the community as it may not be prescribed appropriately or safely.

Given that prescribing of LMWH during pregnancy should not be given at the level of general practice care, but rather after specialist consultation primarily through the hospital system, "improving accessibility" to LMWH is not as relevant to pregnancy.

### *PHARMAC's Response*

It is intended that pregnant women are eligible for funded LMWH 8 weeks post partum (we note that the criteria provides for 52 week authorized funding for pregnant women).

The level of care, diagnosis and treatment for pregnant patients would be determined by the patient's clinician, therefore referral to specialist care would continue as appropriate.

An improvement in accessibility could occur. For example, a pregnant patient with an acute DVT might be referred to a specialist centre. Once under the care of that centre the clinician would then determine how best to provide treatment. If the clinician considers it appropriate ongoing treatment could be collected from a retail pharmacy by the patient, rather than the patient needing to return to the hospital (although prescriptions and monitoring would continue to be controlled by the specialist centre). By shifting its costs to the community

pharmaceuticals budget, the centre could then free up resources for other services.

## **Cancer Patients**

### *Issue Raised in Consultation*

It was questioned as to why the length of entitlement was 12 months when there is no evidence for this and it is not clear as to what treatment should occur after six months (it was noted that the Clot in Cancer Trial used dalteparin for six months and did not show any difference in bleeding or overall survival for LMWH when compared to warfarin, and that the ASCO guidelines are vague and suggest that LMWH should be used for those with 'active cancer' (undefined) and those still receiving chemotherapy).

It was noted that monitoring of malignancy associated VTEs is resource intensive requiring regular platelet and renal function testing.

### *PHARMAC's Response*

We accept that the evidence is indeterminate and that while funding for 12 months treatment is available it would not be a requirement that patients receive this length of treatment if the clinician considers that a different period is appropriate.

We note that the Special Authority system requires a time limit and as there are a number of indications where the length of LMWH use differs we have attempted to pragmatically group a number of them together to simplify the Special Authority criteria, whilst retaining the same (or better) access to funding.

## **Other points**

### *Issue Raised in Consultation*

There was concern about pharmacies being left with part packs and it was questioned as to whether there is any consideration for OP dispensing.

### *PHARMAC's Response*

At this stage we are unsure what the average usage per pharmacy would be and while OP would increase expenditure we are happy to review this issue if pharmacy is being left with stock that is not being used.

## **Other Potential Patient Groups proposed for funding**

### *Issue Raised in Consultation*

It was suggested that the following patient groups should be included on the Special Authority:

- patients on oral anti-coagulation whose INR becomes sub therapeutic, in particular patients with heart valves;
- patients who have complex and dangerous venous thromboembolism conditions;
- patients with heart valve transplants who are either intolerant to warfarin or it is contra-indicated;
- heart valve recipients who need to have their warfarin stopped for a procedure/surgery and are still being warfarinised at discharge;
- patients with arterial thromboses (they are not venous thromboembolism) as it is currently not covered at all under DCS and in vascular departments brachiocephalic artery thrombi can sometimes be seen which may or not be treated surgically but often require enoxaparin for a week or two thereafter;
- other cases which do not come under the surgery criteria ie pelvic fracture where the surgeon requires enoxaparin for 2 weeks post-discharge; and,
- prolonged immobilisation, particularly if additional risk factors are present.

*PHARMAC's Response*

The Special Authority covers at least the current DCS criteria and PHARMAC is open to considering additional patients groups following advice from PTAC. Any information that could be provided in support of the above patients groups would be appreciated.

**More information**

If you have any queries about these changes please contact the PHARMAC helpline on 0800 66 00 50 (9 am to 5 pm weekdays).