Nephrology Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 6 December 2016

(minutes for web publishing)

Nephrology Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.*

Note that this document is not necessarily a complete record of the Nephrology Subcommittee meeting; only the relevant portions of the minutes relating to Nephrology Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Nephrology Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 10 & 11 August 2017, the record is available on the PHARMAC website.

Record of the Nephrology Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC) meeting held at PHARMAC on 6 December 2016

1 Summary of Recommendations

1.1 The Subcommittee considered that pneumococcal, zoster, and hepatitis B vaccines be funded for the above specified patients and patients with CKD Grades 4 and 5 and **recommended** PHARMAC should seek relevant funding applications for these vaccines and indications.

1.2 The Subcommittee reiterated its previous **recommendation** with regards to proposed Special Authority criteria for cinacalcet for secondary and tertiary hyperparathyroidism. The Subcommittee urged PHARMAC to reconsider the funding of cinacalcet and noted its intention to write to PTAC to clarify their concerns regarding the funding of cinacalcet and the proposed clinical criteria to define the target population that would benefit from cinacalcet treatment; and to provide additional evidence to support its use in these settings.

1.3 The Subcommittee **recommended** that levamisole be funded for the treatment of frequently relapsing steroid sensitive nephrotic syndrome (FR SSNS) in paediatric patients with a low priority if a suitable supply is obtained.

1.4 The Subcommittee **recommended** that tolvaptan for patients with autosomal dominant polycystic kidney disease (ADPKD) be listed on the Pharmaceutical Schedule with a high priority if a registered product becomes available.

1.5 The Subcommittee **recommended** that access to enoxaparin be widened to include community dialysis only if cost neutral to the Combined Pharmaceutical Budget.

2 Record of the Previous Nephrology Subcommittee Meeting

2.1 The Subcommittee noted and accepted the record of its previous meeting held on 2 December 2014.

3 Therapeutic Group Review

3.1 The Subcommittee noted a review of funded pharmaceuticals relevant to nephrology provided by PHARMAC staff.

Previous recommendations and action points

3.2 The Subcommittee reviewed a summary of active recommendations and action points from the 2014 Nephrology Subcommittee meeting and the relevant PTAC minutes.

3.3 The Subcommittee noted that PHARMAC was continuing to investigate avenues to secure a supplier of potassium citrate tablets in New Zealand and suggested that Douglas Pharmaceuticals could be approached.

3.4 The Subcommittee noted that the completed recommendations and action points, and those with no further action required, would be removed from the summary list.

Review of funding applications

3.5 The Subcommittee noted a table showing the outstanding funding applications and funding decisions which had been completed since the previous 2014 Subcommittee meeting.

3.6 The Subcommittee noted that widened access to rituximab for paediatric nephrotic syndrome and renal multivitamin for patients on dialysis for patients with CKD Grade 5 were now funded.

3.7 Members noted that tacrolimus for non-transplant indications was recommended as a medium priority by the Transplant Immunosuppressant Subcommittee, and was accepted by PTAC; it is now ranked as an option for investment.

Iron preparations

3.8 The Subcommittee noted that ferric carboxymaltose (Ferinject) was listed in Section H (Hospital Medicines List) with restriction criteria and considered that this agent was used frequently by both nephrologists and gastroenterologists. Members noted that there was currently a national project underway looking at providing access to ferric carboxymaltose infusions in a community setting with various DHBs looking at pilot programme. Members considered that there would need to be a strict pathway and criteria for access, including a laboratory testing pathway and infusion safety criteria, to ensure that general practitioners understand which patients should receive this treatment.

Vitamin D

3.9 The Subcommittee noted that cholecalciferol 1.25 mg tablets were no longer funded because Medsafe's provisional consent for Cal-d-Forte had expired. Members noted that it had been possible to crush the tablets and mix with oil for paediatric patients, however this is not possible with the gelatin capsules. Members noted that caregivers of paediatric patients were using a needle to withdraw the contents of the cholecalciferol capsule for oral administration and this created a risk of needle stick injury and inconsistent dosing. Members noted the Vitadol C preparation containing vitamin D was not suitable for children with renal disease due to the vitamin A content. The Subcommittee noted that PHARMAC had received an application from Douglas Pharmaceuticals for an oral liquid vitamin D supplement and considered that it would be appropriate for PHARMAC to look at funding that presentation.

3.10 The Subcommittee noted that following the 2015/16 annual tender, Calcitriol AFT (0.25 and 1 mcg capsules) was awarded sole supply from 1 November 2016.

Renal multivitamin

3.11 The Subcommittee noted that a multivitamin suitable for patients with renal disease was listed on the Pharmaceutical Schedule from 1 October 2015 subject to Special Authority (SA) criteria and over 2,400 patients had accessed treatment up to September 2016.

Antianaemics, antiplatelets and anticoagulants

3.12 The Subcommittee noted that Eprex became the sole supply brand of erythropoietin alfa from 1 March 2015 until February 2018 and significant savings were achieved.

Oncology and immunosuppressants

Tacrolimus

3.13 The Subcommittee noted that there had been a change to the funded brand of tacrolimus in 2014 which resulted in a 60% price reduction. Members considered that the brand switch had been well managed by PHARMAC and there had been no significant issues.

Herpes virus treatments

3.14 The Subcommittee noted that from 1 January 2016, there had been a significant price reduction on valaciclovir tablets that were now funded without restrictions.

3.15 The Subcommittee noted that there had also been a price decrease on valganciclovir although the SA criteria currently remain in place. The Subcommittee noted that the TISC and the Anti-infective Subcommittee had discussed valganciclovir use during steroid pulse dosing for graft rejection at previous meetings and that PTAC subsequently considered this issue in 2016. Members noted that PTAC had requested that TISC review the evidence in relation to CMV reactivation and treatment/prophylaxis of Epstein-Barr virus at their next scheduled meeting in 2017. Members noted that there had been a recent article published online only in October 2016 regarding the efficacy of valganciclovir for prevention of infections with cytomegalovirus and Epstein-Barr virus after kidney transplant in children (now published as Cameron et al. Pediatr Transplant. 2017 Feb;21(1) that may be helpful.

4 Factors for Consideration

4.1 The Subcommittee noted a presentation by PHARMAC staff outlining PHARMAC's new decision making framework, the Factors for Consideration (FFC), which came into effect on 1 July 2016.

4.2 The Subcommittee noted that the meeting papers it had received were under the FFC framework and all recommendations were to be made with the FFC in mind.

5 Matters Arising

Sodium bicarbonate

5.1 The Subcommittee noted that following communication between PHARMAC and the Nephrology Subcommittee in September 2016, a letter was submitted on behalf of the Subcommittee to Medsafe regarding the clinical need for an oral formulation of sodium bicarbonate. Members had no further comments.

Immunisations with renal disease

5.2 The Subcommittee noted that at its October 2016 meeting, the Immunisation Subcommittee recommended that PHARMAC seek advice from the Nephrology Subcommittee regarding the delivery of vaccines to adult populations with special immunisation requirements in New Zealand and defining which patients with renal disease require additional immunisations and how those patients could be best identified. The Subcommittee considered that chronic kidney disease (CKD) is the most appropriate terminology to use when describing patients with renal disease and the stages of CKD (1-5 based on estimated Glomerular Filtration Rate (GFR)) should be used as appropriate for each vaccine. Members considered that patients with CKD stage 4 (15-30% GFR) and stage 5 (less than 15% GFR or on dialysis) would usually be the patients to target for vaccination and in some instances this could be restricted to patients with CKD 4/5 being worked up for dialysis and/or transplant.

5.3 Members noted it was difficult to estimate the number of patients with CKD 4 and 5 in New Zealand since estimates often include CKD 3. Members estimated there would be around 15,000 people in New Zealand with CKD 4 and 5, however, members noted that rates of CKD would be higher in Maori, Pacific and some Asian populations. Members noted ANZData from 2015 indicates there are around 2,700 patients on renal replacement therapy (dialysis) in New Zealand and approximately 1,600 people who have received a kidney transplant.

5.4 The Subcommittee considered that overall, patients with CKD and renal transplant recipients were well covered with the currently funded vaccines, however, there were some small gaps to be addressed.

5.5 The Subcommittee considered that the current funding restrictions for the influenza vaccination for renal patients with any stage of CKD were appropriate.

5.6 The Subcommittee considered there was limited evidence available regarding the use of pneumococcal vaccination in different stages of CKD, however, Members noted the higher prevalence and morbidity of pneumococcal disease in CKD patients than in the general population. Members noted that evidence suggested that earlier vaccination provided a better response than waiting until a patient had severe CKD. The Subcommittee considered that funded access to pneumococcal vaccine should be widened to include patients with CKD stage 4 (15-30% GFR) and stage 5 (less than 15% GFR or on dialysis).

5.7 The Subcommittee noted that hepatitis B vaccine is funded for dialysis and transplant patients, however, is not currently funded for patients with CKD.

Members noted that it was important to be immunised against hepatitis B prior to starting dialysis and/or undergoing transplantation and considered that vaccinating those patients was likely already happening. Members noted that seroconversion is generally better in patients with higher renal function. The Subcommittee considered that funded access to hepatitis B vaccine should be widened to include patients with CKD Stage 4 and 5.

5.8 The Subcommittee noted the zoster vaccine is not currently funded in New Zealand and is currently under consideration by PHARMAC. Members noted that zoster vaccine should be considered for patients with CKD stage 4 and 5 if it available in the future.

5.9 The Subcommittee noted that Member Tonya Kara had information on the work completed with the Immunisation Advisory Centre (IMAC) defining transplant patients for the purpose of immunisations, which included the following:

- Patients considered for dialysis
- Patients on dialysis
- Patients on the transplant list
- Patients in work-up for transplant
- Patients post-transplant

5.10 The Subcommittee considered that pneumococcal, zoster, and hepatitis B vaccines be funded for the above specified patients and patients with CKD Grades 4 and 5 and **recommended** PHARMAC should seek relevant funding applications for these vaccines and indications.

Cinacalcet

5.11 The Subcommittee noted a paper from PHARMAC staff updating the Subcommittee on the status of consideration of funding for cinacalcet for patients with parathyroid disorders.

5.12 The Subcommittee noted that PHARMAC had sought advice primarily due to the receipt of a significant number of NPPA applications for cinacalcet. Members noted the PHARMAC staff had previously sought advice on a number of occasions from PTAC and its relevant Subcommittees regarding cinacalcet.

5.13 The Subcommittee noted that PTAC had recommended that all indications other than parathyroid carcinoma and calciphylaxis be declined based on a lack of good quality evidence to support the use of cinacalcet in improving clinically important outcomes in these patient groups. Members noted the indications PTAC recommended for decline included primary, secondary and tertiary hyperparathyroidism with symptomatic hypercalcaemia including those patients contraindicated to surgery or where previous surgery has been unsuccessful and regardless of whether or not the patient is on dialysis.

5.14 The Subcommittee noted that cinacalcet was listed on the Pharmaceutical Schedule from 1 May 2016 for the treatment of parathyroid carcinoma or calciphylaxis subject to Special Authority criteria, which had been developed taking into account previous advice from both the Endocrinology and Nephrology Subcommittees. Several members were not aware of the proposal for funding and

did not see the consultation document, however, PHARMAC staff confirmed that it was sent to the Nephrology Subcommittee.

5.15 The Subcommittee noted that since cinacalcet was listed on the Pharmaceutical Schedule in May 2016, NPPA was no longer a funding pathway for new patients to obtain funded cinacalcet. Members noted that patients with severe tertiary hyperparathyroidism, who would previously have been approved funding via the NPPA pathway, were no longer able to access NPPA funding and this created an inequity of access for new patients who were unable to access treatment while existing patients could.

5.16 Members considered that the funding criteria proposed by the Nephrology Subcommittee at its December 2014 meeting were very sensible but were not reflected in the current Special Authority for cinacalcet.

5.17 The Subcommittee considered that the current Special Authority criteria for cinacalcet for calciphylaxis were not appropriate. Members considered that there was no evidence for the use of sodium thiosulfate or bisphosphonates in the treatment of calciphylaxis and it was illogical to have this as a prerequisite to trial prior to getting cinacalcet. Members considered there was more evidence for the use of cinacalcet than sodium thiosulfate or bisphosphonates in this indication. Members also raised concerns regarding the requirement for a calcium level of 3.0 mmol/L or greater as levels this high rarely occur with calciphylaxis. Members considered that the use of calcium based phosphate binders in New Zealand exacerbates the rate of calciphylaxis in the New Zealand renal population, however, the availability of a non-calcium phosphate binder would not remove the clinical need for a calciphylaxis treatment.

5.18 The Subcommittee considered there were several other patient groups that should be considered or reconsidered for funding of cinacalcet: post renal transplant patients with severe hypercalcaemia requiring treatment as a bridge to parathyroidectomy; symptomatic patients with tertiary hyperparathyroidism as bridge to parathyroidectomy; and symptomatic patients with tertiary hyperparathyroidism where parathyroidectomy is contraindicated.

5.19 The Subcommittee reiterated its previous **recommendation** with regards to proposed Special Authority criteria for cinacalcet for secondary and tertiary hyperparathyroidism. The Subcommittee urged PHARMAC to reconsider the funding of cinacalcet and noted its intention to write to PTAC to clarify their concerns regarding the funding of cinacalcet and the proposed clinical criteria to define the target population that would benefit from cinacalcet treatment; and to provide additional evidence to support its use in these settings.

6 Levamisole

Application

6.1 The Subcommittee reviewed a clinician's funding application for levamisole in frequently relapsing steroid sensitive nephrotic syndrome.

Recommendation

6.2 The Subcommittee **recommended** that levamisole be funded for the treatment of frequently relapsing steroid sensitive nephrotic syndrome (FR SSNS) in paediatric patients with a low priority if a suitable supply is obtained.

6.3 The Subcommittee noted that the applicant, Dr William Wong, was not present in the room during the recommendation discussion and voting process.

Discussion

6.4 The Subcommittee noted that levamisole was not included on the Hospital Medicines List (HML) during its establishment. In 2014, Members of the Nephrology Subcommittee provided feedback that levamisole was an effective treatment for FR SSNS, and it was noted that levamisole had been withdrawn from the market worldwide due to rare but serious side-effects, including agranulocytosis. Members noted that levamisole is not registered in New Zealand and it is unlikely that PHARMAC would be able to source a supplier give the small market and global supply status.

6.5 The Subcommittee noted that PHARMAC has received three NPPA applications for its use in nephrotic syndrome, with the aim of reducing steroid use. Members noted a recent application was not progressed as it was considered it did not meet the principles of the NPPA policy in that not all funded alternative had been tried.

6.6 Members noted that rituximab was recently listed on the HML for the treatment of nephrotic syndrome.

6.7 The Subcommittee considered the evidence for the use of levamisole in paediatric patients in a 2013 Cochrane review (Non-corticosteroid treatment for nephrotic syndrome in children, Pravitsitthikul et al. Cochrane Database of Systematic Reviews 2013, Issue 10, CD002290) which summarised that 8-week courses of cyclophosphamide or chlorambucil and prolonged courses of ciclosporin and levamisole reduce the risk of relapse in children with relapsing SSNS compared to corticosteroids alone. Members noted that limited data indicate that mycophenolate mofetil and rituximab are valuable additional medications for relapsing SSNS.

6.8 The Subcommittee considered that overall the evidence was limited. The Subcommittee considered the following studies in regards to levamisole and other treatments for FR SSNS such as cyclophosphamide, ciclosporin, tacrolimus and rituximab:

- Elmas et al (Int Urol Nephrol 2013;45:1047-55)
- Ekambram et al. (Indian Paediatrics 2014;51:371-3)
- Al-Saran et al. (Pediatri Nephrol 2006;21:201-5)
- Donia et al. (Pediatric Nephrol 2002;17:355-358)
- Bagga et al. (Pediatri Nephrol 1997;11:415-7)
- British Association for Paediatric Nephrology (Lancet 1991;337:8757)
- Boyer et al.(Pediatric Nephrol 2008;23:575-80)
- Mongeau et al. (Peditric Nephrol 1998;2:398-401)
- Davin et al. (Peditri Nephrol 2005;20:10-4)

- Jiang et al. (Clinical Science 2015;128:883-93).

6.9 The Subcommittee considered that children with FR SSNS would benefit most from levamisole since it would provide another option to help reduce corticosteroid use and delay using treatments that may impact fertility in the longer term (e.g. cyclophosphamide).

6.10 The Subcommittee considered that there would be a very small number of patients, between 5 and 10 per year, and that there was no disproportionally affected population group with FR SSNS. The Subcommittee considered that levamisole was a cheap drug to manufacture and generally well tolerated. Members noted the that India have a supply of levamisole and therefore many of the studies regarding levamisole are completed there.

6.11 Members noted that levamisole appeared to be no more dangerous than other options with additional benefits of less adverse effects, such as no loss of hair, that can occur with other treatments. Members noted that serious haematological adverse effects were extremely rare in paediatric patients with nephrotic syndrome since levamisole is used in low doses with close monitoring.

6.12 The Subcommittee considered that mycophenolate was a possible funded alternative for this group but noted there were no studies comparing it to levamisole.

6.13 The Subcommittee noted that without a registered product in New Zealand, it would be difficult to secure a stable supply of levamisole and suppliers were unlikely to register their product in New Zealand due to the very small market. Members noted that it would be important to obtain a quality product. Members noted that levamisole had a short shelf life, making it impractical to source bulk supplies. Members considered that the Subcommittee could revisit the application to define funding criteria only once the supply issue had been sorted.

7 Tolvaptan

Application

7.1 The Subcommittee reviewed a clinician's funding application for tolvaptan tablets for patients with autosomal dominant polycystic kidney disease (ADPKD).

Recommendation

7.2 The Subcommittee **recommended** that tolvaptan for patients with autosomal dominant polycystic kidney disease (ADPKD) be listed on the Pharmaceutical Schedule with a high priority if a registered product becomes available.

Discussion

7.3 The Subcommittee noted that ADPKD is a complex, progressive, systemic genetic condition characterised by an increase in the number and size of fluid-filled cysts

in the kidney resulting in urine concentration defects, hypertension, acute and chronic pain, kidney stones, haematuria, cyst and urinary tract infections, and, most importantly, renal function loss. Members noted the renal failure occurs in approximately 70% of patients with ADPKD before the age of 60 years.

7.4 The Subcommittee noted that tolvaptan was a novel treatment for ADPKD and there were currently no alternative treatments for those patients outside of pain management and lifestyle changes to increase fluid intake and reduce blood pressure. Members noted the primary trial, Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and its Outcomes (TEMPO) 3:4 trial which was a Phase III, international multicentre, randomised, double blind and placebo-controlled study in 1445 patients treated with tolvaptan for 3 years (Torres et al. NEJM 2012;367:2407-18).

7.5 The Subcommittee noted the primary endpoint in the TEMPO 3:4 study was annualised rate of total kidney volume (TKV) change. Secondary endpoints included a composite endpoint of time to multiple composite ADPKD-related events (worsening kidney function, kidney pain, hypertension, and albuminuria) and rate of kidney function decline. Members noted Torres et al reported that tolvaptan significantly reduced the rate of increase in TKV by approximately 50% compared with a placebo: 2.80% per year (95% CI 2.5-3.1) vs. 5.51% per year (95% CI 5.1 – 6.0; P<0.001). Members noted that results also demonstrated a 33% reduction in rate of glomerular filtration rate (GFR) loss in this high-risk group and that other symptoms such as pain and infections were also reduced. Members noted the composite end point favoured tolvaptan over placebo (44 vs. 50 events per 100 follow-up-years, P = 0.01), with lower rates of worsening kidney function (2 vs. 5 events per 100 person-years of follow-up, P<0.001) and kidney pain (5 vs. 7 events per 100 person-years of follow-up, P = 0.007). The Subcommittee estimated that pain was reduced by 8% and also noted a reduction in haematuria was reported.

7.6 The Subcommittee considered that the study was very encouraging but had limitations. Members noted that patients over 50 years of age were not included in the study, and the majority of participants were Caucasian. Members noted 77% of participants completed the trial and there was a higher discontinuation rate in the tolvaptan group due to adverse effects. Members considered that the data is very early and a second trial backing up the results of TEMPO would be reassuring. Members considered that data in children is also needed.

7.7 The Subcommittee considered that the use of tolvaptan had the potential to delay dialysis by 4-7 years in people with ADPKD which would result in significant savings to the health system and may also lower mortality rates. Members estimated that dialysis was delayed by about 1 year for every 4 years of treatment with tolvaptan. Members considered that the rate of mortality for a 30-year old patient on dialysis was the same as an 80-year-old in the general population. Members further considered that the data showed a life extension of 2.5 years.

7.8 The Subcommittee noted a post hoc analysis (Torres et al Clin J Am Soc Nephrol 2016;11(5):803-11) was performed to reassess the primary and secondary efficacy endpoints by CKD stage at baseline. The analysis suggests clinically similar beneficial effects of tolvaptan in ADPKD across CKD stages 1–3.

7.9 The Subcommittee considered that patients with ADPKD CKD stages 2 and 3 with large kidneys would benefit most from treatment with tolvaptan. The Subcommittee considered that it was sufficient to use ultrasound to determine kidney volume. Members considered that older patients with comorbidities that prevent dialysis may particularly benefit. The Subcommittee considered the long-term duration of effect and prevention of harm from tolvaptan treatment is yet to be proven.

7.10 The Subcommittee noted that the FDA released a drug safety communication in 2013 regarding the use of tolvaptan for treatment of hyponatraemia which recommended treatment should be no longer than 30 days for this indication. Members noted that hepatotoxicity has been observed in some people receiving tolvaptan for ADPKD.

7.11 The Subcommittee considered the applicant's patient numbers may be an overestimate. The Subcommittee considered there is limited data currently available regarding the incidence of ADPKD in New Zealand, however, estimated there would be an incident population of approximately 25 patients per year.

7.12 The Subcommittee considered that the disease was rare in Māori and predominantly affected Europeans. The Subcommittee considered that the disease predominantly affected patients between the age of 18-50 year old but occasionally children were affected.

7.13 Members noted that international pricing of tolvaptan was very expensive. Members noted that people with ADPKD would usually have specialist follow up on an annual basis and if tolvaptan treatment was available, more regular follow-up would be required.

7.14 The Subcommittee considered that there was no other effective pharmaceutical treatment for this population and the appropriate comparator was placebo. However, around 5% of the group would require a nephrectomy to relieve symptoms.

7.15 The Subcommittee considered that this treatment could have a significant positive psychological impact on both patients and their families as the condition involved agonising pain and the knowledge that they would need to be on dialysis at some point in the future. Members considered that it was incredibly rare to find a treatment which could delay the rate of kidney dysfunction.

7.16 The Subcommittee noted that based on the currently available evidence, there was no reason to think that tolvaptan would help with polycystic liver disease (PLD) and considered that the prevalence of PLD was no higher in patients with ADPKD than in the general population.

7.17 The Subcommittee noted that New Zealand had one of the lowest kidney donation rates in the world with approximately 600 patients on the waiting list and considered that any treatment that delayed dialysis and the need for a transplant would free up more kidneys on an annual basis.

7.18 The Subcommittee noted that tolvaptan is not currently registered in New Zealand and PHARMAC intend to discuss a possible submission to Medsafe with the supplier.

7.19 The Subcommittee noted that funding of tolvaptan would not be further considered by PHARMAC until the product had Medsafe approval and a funding application was received from the supplier, Otsuka Pharmaceuticals, and reviewed by PTAC along with the minutes from this discussion.

8 Enoxaparin

Application

8.1 The Subcommittee reviewed a funding application from Sanofi New Zealand for widened access to enoxaparin sodium via community pharmacy for people undergoing haemodialysis at home or in a community setting.

Recommendation

8.2 The Subcommittee **recommended** that access to enoxaparin be widened to include community dialysis only if cost neutral to the Combined Pharmaceutical Budget.

Discussion

8.3 The Subcommittee noted that enoxaparin sodium is currently listed in the Hospital Medicines List (HML) unrestricted, which means it funded for any indication, including haemodialysis, within DHB hospitals. The Subcommittee noted that in the community setting access to enoxaparin sodium is currently restricted by Special Authority restrictions which do not include use during haemodialysis. The current criteria limit the long-term use of enoxaparin sodium to pregnant women or those who require venous thromboembolism treatment in the context of malignancy.

8.4 The Subcommittee noted that enoxaparin sodium is not currently widely used for haemodialysis in the hospital setting, even though this would be possible, due to a higher perceived cost compared with unfractionated heparin.

8.5 The Subcommittee noted that recent price reductions for enoxaparin sodium may make it more cost-effective versus unfractionated heparin. The Subcommittee noted that despite the price reductions, complete removal of the Special Authority restrictions in the community is not currently considered a priority for PHARMAC funding due to a likely considerable increase in expenditure without strong evidence of additional clinical benefits.

8.6 The Subcommittee noted that there were no problems currently with accessing heparin in the community.

8.7 The Subcommittee noted Māori are disproportionally affected by end stage kidney disease and thus have higher rates of haemodialysis, although lower rates of home haemodialysis compared to the non-indigenous population.

8.8 The Subcommittee noted Pacific peoples are disproportionally affected by end stage kidney disease and thus have higher rates of haemodialysis, although lower rates of home haemodialysis compared to the non-indigenous population, despite some small improvements in home dialysis rates in recent years.

8.9 The Subcommittee reviewed the evidence for the use of enoxaparin during haemodialysis and considered the CARI Guidelines (Dialysis Adequacy – Haemodialysis. 2005) and the following studies provided the main evidence for its use as a suitable alternative to unfractionated heparin:

- Palamaner Subash Shantha et al. PeerJ. 2015;3:e835
- Davenport A. Nephrology 2009;14:455–461
- Kessler et al. Semin Dial. 2015;28:474-89
- Kurtkoti et al. Nephrology. 2016;21:663-68
- Suranyi & Chow. Nephrology. 2010;15:386–92
- Lim et al. J Am Soc Nephrol. 2004;15:3192–3206

8.10 The Subcommittee noted that overall there was little evidence of sufficient quality to support an additional benefit for using enoxaparin sodium. The Subcommittee considered that enoxaparin sodium could be considered to have the same or similar efficacy and safety as unfractionated heparin during haemodialysis.

8.11 The Subcommittee did, however, note that enoxaparin sodium was possibly easier to administer given that only one bolus injection was sufficient to cover most session durations. The Subcommittee considered that widened access in the community setting may simplify the process and make it somewhat easier for patients to move to community based haemodialysis. The Subcommittee considered the actual benefit to individuals and health services would be small, however it was plausible that one or two extra patients may move to home haemodialysis.

8.12 The Subcommittee noted that haemodialysis in a hospital setting cost approximately $78,000 per year per patient while at-home or community based haemodialysis cost approximately $30,000 per year per patient, which meant any shift of patients to community haemodialysis would result in a savings to DHBs.

8.13 The Subcommittee considered the dose of enoxaparin used in clinical practice is likely lower than the dose of 1 mg/kg administered into the arterial circuit recommended in the Clexane Data Sheet, and is more likely to align with a dose of 0.3 - 0.5 mg/kg administered into the venous circuit at the start of the dialysis session as specified in the Gold Coast Hospital and Health Service protocol (Work

Instruction, Version No.2;2016:1-5), with visual only monitoring of the dialysis circuit sufficient to determine if an additional dose is required.

8.14 The Subcommittee considered the following modifications to the initial and renewal Special Authority criteria were clinically appropriate (additions in bold, deletions in strikethrough).

INITIAL APPLICATION – Pregnancy**,** ~~or~~ Malignancy **or Haemodialysis**
Applications from any relevant practitioner. Approvals valid for 1 year.
Prerequisites

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**; or**
3. **For the prevention of thrombus formation in the extra-corporeal circulation during home haemodialysis**

INITIAL APPLICATION - Venous thromboembolism other than in pregnancy or malignancy
Applications from any relevant practitioner. Approvals valid for 1 month.
Prerequisites

1. For the short-term treatment of venous thromboembolism prior to establishing a therapeutic level of 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 oral anticoagulant 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 - Pregnancy**,** ~~or~~ Malignancy **or Haemodialysis**
Applications from any relevant practitioner. Approvals valid for 1 year.
Prerequisites

1. Low molecular weight heparin treatment is required during a patient's pregnancy; or
2. For the treatment of venous thromboembolism where the patient has a malignancy**; or**
3. **For the prevention of thrombus formation in the extra-corporeal circulation during home haemodialysis**

RENEWAL - Venous thromboembolism other than in pregnancy or malignancy
Applications from any relevant practitioner. Approvals valid for 1 month.
Prerequisites

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)