Record of the Haematology Advisory Committee Meeting held on 9 November 2022

This meeting was held as *hybrid,* both in-person and virtually

Haematology Advisory Committee records are published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Haematology Advisory Committee meeting; only the relevant portions of the meeting record relating to Haematology Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Haematology Advisory Committee 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.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Brian Anderson (Chair)
Paul Harper
Eileen Merriman
Paul Ockelford
Julia Phillips
Lochie Teague

Apologies
None

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• apixaban within the context of haematology treatments, for people requiring anticoagulation therapy.	Medium
• apixaban within the context of haematology treatments for people with ESRD or intolerance of other funded DOAC's	High
• desmopressin acetate (DDAVP) 15mcg/mL vial be funded in the community for management of acute bleeding or prophylaxis for minor surgery in people with moderate and mild Haemophilia A, von Willebrand Disease or inherited platelet disorders	High
• ferric carboxymaltose in the community be widened for the treatment of iron-deficiency anaemia with chronic inflammatory disease	High

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Haematology Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and Specialist Advisory Committees 2021, available on the Pharmac website at https://pharmac.govt.nz/assets/2021-Specialist-Advisory-Committee-Terms-of-Reference.pdf The Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 7.2 of the PTAC Terms of Reference.

3.3. The Haematology Advisory Committee is a Specialist Advisory Committee of Pharmac. The Haematology Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Haematology Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Haematology that differ from PTAC's, including the priority assigned to

recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Haematology that differ from the Haematology Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Haematology Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Haematology.

4. Welcome and Introduction

4.1. The Chair welcomed the Committee.

5. Record of previous Haematology meeting held Monday, November 29, 2021

5.1. The Advisory Committee reviewed the record of the Haematology meeting held on Monday November 29 2021 and agreed that the record be accepted.

6. Correspondence and Matters Arising

Commercial options for direct-acting oral anticoagulants (DOACs)

Application

6.1. The Committee reviewed a request from Pharmac seeking advice regarding the clinical need to inform commercial options for direct-acting oral anticoagulants (DOACs).

6.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

6.3. The Committee **recommended** that apixaban be listed without restriction with a **medium** priority within the context of haematology treatments.

6.4. In making this recommendation, the Committee considered:

- The evidence demonstrating that apixaban provides a health benefit in those requiring anticoagulation treatment with an improved safety profile compared to currently funded DOACs.

6.5. The Committee **recommended** that apixaban be listed with a **high** priority within the context of haematology treatments, subject to the following Special Authority criteria:

INITIAL APPLICATION
Applications from any relevant practitioner. Approvals valid for 12 months.
All of the following:
1. Either:
   1.1. Patient has end stage renal disease (ESRD) with an eGFR of less than 30ml/min; or
   1.2 Patient has experienced intolerable side effects following a trial of dabigatran and rivaroxaban

RENEWAL
Applications from any relevant practitioner. Approvals valid for 12 months.
The treatment remains appropriate, and the patient is benefiting from treatment

Discussion

Background

6.6. The Committee noted that dabigatran and rivaroxaban are currently funded by Pharmac (without restriction). The Committee noted that Pharmac has received two previous funding applications for apixaban:

- Prevention of venous thromboembolic events (VTE) following major orthopaedic surgery: The Committee noted that this application was declined as part of Pharmac's decision to decline inactive funding applications.
- Stroke prevention in atrial fibrillation: The Committee noted that this application is currently under the status "options compared" and that due to funding of rivaroxaban, apixaban was moved from the OFI to the cost-neutral list in June 2018.

The Committee noted that, in 2016 and 2017, the Haematology Subcommittee considered commercial options for the DOAC market. The Committee noted that, at that time, the only DOAC listed on the Pharmaceutical Schedule was dabigatran and the Subcommittee considered that switching from one DOAC to another would not be clinically unreasonable. The Committee noted that the Subcommittee further considered that funding only one DOAC would be reasonable if the DOAC was well tolerated by the majority using it, and providing a second DOAC would be available for the group of individuals for whom the associated side effects were intolerable.

6.7. The Committee noted the Subcommittee considered that if only one DOAC was to be funded, apixaban would be preferred over rivaroxaban based on the evidence for slightly lower bleeding rates with equivalent efficacy. The Committee noted that at this time, it was considered that both factor Xa inhibitors (apixaban, rivaroxaban) would be preferred over dabigatran, primarily due to lower renal clearance and reduced gastrointestinal adverse effects. The Committee noted that the Subcommittee recommended another DOAC be funded for those unable to take dabigatran, especially those with poor renal function, with a medium priority.

6.8. The Committee noted that following on from the recommendations received for apixaban, and the open listing of both dabigatran and rivaroxaban, the application to list apixaban was identified by Pharmac staff as an inactive application that could be progressed to a decline decision. The Committee noted that a consultation document was released in 2020, proposing to formally decline apixaban, however based on the consultation feedback and additional evidence provided by respondents, the application to list apixaban for stroke prevention in atrial fibrillation was not declined, pending further clinical advice.

Health need

6.9. The Committee noted that the health need of those requiring DOACs for prevention or treatment of coagulation disorders has been discussed in previous clinical advice meetings.

6.10. The Committee noted that apixaban is licensed for venous thromboembolism (VTE) treatment and prevention, including cancer-associated thrombosis (CAT) and stroke prevention in atrial fibrillation (AF). The Committee noted that dabigatran and rivaroxaban are approved for the same indications, although there are no trials available for the use of dabigatran in CAT.

6.11. The Committee considered that there is an unmet health need in several groups requiring treatment with DOACs. The Committee considered that there is a health need for those in which dabigatran and rivaroxaban are contraindicated due to

recent gastrointestinal (GI) bleeding or at significant risk of GI bleeding. The Committee noted that apixaban trials show no increase in GI bleeding when compared with warfarin and so could be used in this setting. The Committee considered that all DOACs are preferable to warfarin due to reduction in intracranial haemorrhage (ICH) (Wolfe et al. J Throm Haemost. 2018;16:1296-1306) and ease of use (ie no need for laboratory monitoring).

6.12. The Committee considered that there is a health need for those with End Stage Renal Disease (ESRD) and/or those on haemodialysis, as the only currently funded option for the individuals is warfarin. The Committee noted that dabigatran can be used if creatinine clearance (CrCl) is ≥30 mL/min, and rivaroxaban can be used if CrCl ≥15 mL/min. However, the Committee considered that most clinicians are reluctant to use more than 15 mg of rivaroxaban if CrCl <30 mL/min. The Committee considered that emerging data on apixaban suggests it would be a good option for those with ESRD and could then replace warfarin in that setting.

6.13. The Committee considered there is also a health need for those of childbearing age in which rivaroxaban can cause heavy menstrual bleeding. The Committee considered that although dabigatran is less likely to cause this, GI side effects preclude its use in at least 10% of individuals. The Committee noted that approximately 15% of patients discontinued dabigatran by 1 year in the RELY trial (Connolly et al, N Engl J Med 2009; 361:1139-1151), and that approximately 12% experienced dyspepsia and approximately 7% experienced diarrhoea. The Committee considered that this is very close to what is seen in clinical practice.

6.14. The Committee considered that, if apixaban were to be funded, there is likely to be an ongoing need for warfarin for certain groups of people, as warfarin will still be required in individuals with triple positive antiphospholipid syndrome and mechanical heart valves.

Health benefit

6.15. The Committee noted that dabigatran is a direct thrombin inhibitor, and rivaroxaban and apixaban are a direct inhibitors of factor Xa, thereby interrupting the blood coagulation cascade and inhibiting both thrombin formation and thrombus development (PRADAXA Medsafe datasheet. DOR Mar 2020; XARELTO Medsafe datasheet. DOR May 2021; ELIQUIS Medsafe datasheet. DOR Aug 2019).

6.16. The Committee noted the following evidence received in response to the proposal to decline apixaban:

6.16.1. The Committee noted a meta-analysis including 5 RCTs investigating an outcome of stroke or systemic embolism for elderly patients (≥75 years) taking DOACs (apixaban, edoxaban, rivaroxaban, and dabigatran). The Committee noted that apixaban ranked the best in efficacy with regard to the measured endpoints of prophylactic prevention of stroke and systemic embolism followed by rivaroxaban, edoxaban, dabigatran, and warfarin. The Committee noted that, with regard to safety as measured by major bleeding, apixaban also ranked the best followed by edoxaban, dabigatran, warfarin, and rivaroxaban (Deng et al. Front Med. 2020;7:107).

6.16.2. The Committee noted a retrospective cohort study comparing the safety and efficacy of apixaban (n=59,172) versus rivaroxaban (n=40,706) for patients with non-valvular AF. The Committee noted that the primary effectiveness outcome was a composite of ischaemic stroke or systemic embolism while the primary safety outcome was a composite of ICH or GI bleeding. The Committee noted that the

incidence rate of ischaemic stroke or systemic embolism was 6.6 per 1000 person years for apixaban versus 8.0 for rivaroxaban (hazard ratio [HR] 0.82, 95% confidence interval [CI] 0.68 to 0.98). The Committee noted that apixaban patients had composite bleed rate of 12.9 per 1000 person years compared to 21.9 for rivaroxaban (HR 0.58, 95% CI 0.52 to 0.66) (Fralick et al. Ann Intern Med. 2020; 172:463-473).

6.17. The Committee noted the following seven publications that provide evidence for the health benefits of DOACs:

6.17.1. A systematic review and meta-analysis including 15 studies of patients with nonvalvular AF who were aged >18 years treated with dabigatran, rivaroxaban, or apixaban for stroke prevention. The Committee noted that the risk of stroke or systemic embolism was similar between rivaroxaban and dabigatran (HR=1.00, 95% CI 0.91 to 1.10; evidence quality: low). The Committee noted that there were no differences in risk of stroke or systemic embolism were observed between rivaroxaban versus apixaban, and apixaban versus dabigatran. The Committee noted that rivaroxaban was associated with a higher risk of major bleeding compared with dabigatran (HR=1.39, 95% CI 1.28 to 1.50; evidence quality: moderate), and a significantly higher risk of major bleeding compared with apixaban (HR=1.71, 95% CI 1.51 to 1.94). The Committee noted that apixaban was associated with lower risk of major bleeding compared with dabigatran (HR=0.80, 95% CI 0.68 to 0.95; evidence quality: low) and was found to have the most favourable safety profile amongst the three DOACs in this study (Li et al. Eur J Epidemiol. 2019;34:173-190).

6.17.2. A systematic review and meta-analysis of 21 observational studies of patients with AF treated with dabigatran, rivaroxaban, or apixaban. The Committee noted that apixaban was associated with lower major and GI bleeding compared with rivaroxaban (HR=2.0, 95% CI 1.6 to 2.5) and dabigatran (HR=1.6, 95% CI 1.3 to 2.1.The Committee noted that dabigatran and apixaban had a similar association with haemorrhagic stroke, but apixaban reduced the level of stroke better than rivaroxaban (HR=1.8, 95% CI 1.1 to 3.0). The Committee noted that apixaban had a similar association with rivaroxaban and dabigatran for ICH, the latter drug performing better than rivaroxaban (HR=1.3, 95% CI 1.0 to 1.7). (Menichelli et al. Eur Heart J Cardiovasc Pharmacother. 2021;7:f11-f19).

6.17.3. A systematic review of 17 randomised controlled trials in patients treated with dabigatran (n=16,074), rivaroxaban (n=14,157), apixaban (n=19,495), and edoxaban (n=11,652). The Committee noted that dabigatran 110 mg ranked as the safest drug (surface under the cumulative ranking curve, 0.85) and reduced the risk of ICH by 56% compared to rivaroxaban (odds ratio [OR]=0.44; 95% credible interval 0.22 to 0.82). The Committee noted that pairwise meta-analysis validated these findings, showing that DOACs were safer than warfarin (OR=0.46; 95% CI 0.35 to 0.59). The Committee noted that the subgroup analysis showed that the benefit was present when DOACs were used in non-valvular atrial fibrillation (OR=0.51; 95% CI 0.38 to 0.68) or VTE (OR=0.32; 95% CI 0.18 to 0.58). The Committee noted that the study concluded that dabigatran 110 mg may be the safest choice among any anticoagulant regarding risk of ICH, and that both dabigatran 110 mg and 150 mg

were safer than rivaroxaban (Wolfe et al. J Thromb Haemost. 2018;16:1296-1306).

6.17.4. A meta-analysis of 29 randomised controlled trials and 4 observational population studies in patients treated with warfarin, enoxaparin, apixaban, dabigatran, edoxaban, or rivaroxaban. The Committee noted that, compared with warfarin, apixaban showed a decreased the risk of major GI bleeding (relative risk [RR] 0.54, 95% CI 0.25 to 0.76), and rivaroxaban tended to increase this risk (RR 1.40, 95% CI 1.06 to 1.85). The Committee noted that dabigatran (RR 1.25, 95% CI 0.98 to 1.60), edoxaban (RR 1.07, 95% CI 0.69 to 1.65), and enoxaparin (RR 1.24, 95% CI 0.63 to 2.43) did not significantly increase the risk of GI bleeding than did warfarin. The Committee noted that in the subgroup analysis, according to indications, apixaban showed a decreased risk of major GI bleeding (RR 0.50, 95% CI 0.34 to 0.74) than did warfarin in AF studies. The Committee noted that dabigatran (RR 2.36, 95% CI 1.55 to 3.60) and rivaroxaban (RR 1.75, 95% CI 1.10 to 6.41) increased the risk of major GI bleeding compared to apixaban (Oh et al. Medicine (Baltimore). 2021;100:e25216).

6.17.5. A systematic review and meta-analysis of28 randomised controlled trials of patients treated with warfarin, enoxaparin, apixaban, dabigatran, edoxaban, or rivaroxaban. The Committee noted that after accounting for dose, rivaroxaban 20 mg, dabigatran 300 mg and edoxaban 60 mg daily had 47%, 40%, and 22% higher rates of major GI bleeding versus warfarin, respectively. The Committee noted that apixaban 5 mg twice daily had lower major GI bleeding compared to dabigatran 300 mg (OR, 0.63; 95% CI, 0.44 to 0.88) and rivaroxaban 20 mg (OR, 0.60; 95% CI, 0.43 to 0.83) daily. The Committee noted that DOACs at standard dose, except apixaban, had a higher risk of major GI bleeding compared to warfarin. The Committee noted that apixaban had a lower rate of major GI bleeding compared to dabigatran and rivaroxaban (Radadiya et al. Eur J Gasterenterol Hepatol. 2021;33:e50-e58).

6.17.6. A systematic review and meta-analysis of 16 observational real-world studies comparing apixaban with other oral anticoagulant drugs. The Committee noted that, compared with warfarin, apixaban regular dose was more effective in reducing any thromboembolic event (OR=0.77; 95% CI 0.64 to 0.93), but no significant difference was found for stroke risk. The Committee noted that apixaban was as effective as dabigatran and rivaroxaban in reducing thromboembolic events and stroke. The Committee noted that the risk of major bleeding was significantly lower for apixaban compared with warfarin, dabigatran, and rivaroxaban (RR reduction, 38%, 35%, and 46%, respectively). The Committee noted that, similarly, the risk for ICH was significantly lower for apixaban than warfarin and rivaroxaban (46% and 54%, respectively) but not dabigatran. The Committee noted that the risk of GI bleeding was lower with apixaban when compared with all oral anticoagulant agents (P<0.00001 for all comparisons) (Proietti et al. Stroke. 2018;49:98-106).

6.17.7. A systematic review and network meta-analysis of 23 randomised controlled trials (n=94,656) in patients taking warfarin, edoxaban, apixaban, dabigatran, or rivaroxaban for prevention of stroke in AF.

The Committee noted that the risk of stroke or systemic embolism was higher with edoxaban 60 mg once daily (1.33, CI 1.02 to 1.75) and rivaroxaban 20 mg once daily (1.35, CI 1.03 to 1.78) than with dabigatran 150 mg twice daily. The Committee noted that the risk of major bleeding was higher with dabigatran 150 mg twice daily than apixaban 5 mg twice daily (1.33, CI 1.09 to 1.62), rivaroxaban 20 mg once daily than apixaban 5 mg twice daily (1.45, CI 1.19 to 1.78), and rivaroxaban 20 mg once daily than edoxaban 60 mg once daily (1.31, CI 1.07 to 1.59). The Committee noted that apixaban 5 mg twice daily was ranked the highest for most outcomes and was cost effective compared with warfarin (López-López et al. BMJ. 2017;359:j5058; with correction for rivaroxaban dosing).

6.18. The Committee was also made aware of the following studies:

6.18.1. The Committee noted a retrospective cohort study in patients with ESRD and AF undergoing dialysis (n=25,523). The Committee noted that the results showed that apixaban was associated with a significantly lower risk of major bleeding (HR=0.72; 95% CI, 0.59 to 0.87; *P*<0.001) compared with warfarin. The Committee noted that standard-dose apixaban (5 mg twice a day; n=1034) was associated with significantly lower risks of stroke/systemic embolism and death as compared with either reduced-dose apixaban (2.5 mg twice a day; n=1317; HR=0.61; 95% CI, 0.37 to 0.98; *P*=0.04 for stroke/systemic embolism; HR=0.64; 95% CI, 0.45 to 0.92; *P*=0.01 for death) or warfarin (HR=0.64; 95% CI, 0.42 to 0.97; *P*=0.04 for stroke/systemic embolism; HR=0.63; 95% CI, 0.46 to 0.85; *P*=0.003 for death) (Konstantinos et al. Circulation. 2018;138:1519-29).

6.18.2. The Committee also noted randomised control data on apixaban, dabigatran, and rivaroxaban. The Committee noted that apixaban showed a 30% reduction in major bleeding when compared with warfarin (compared to 20% in the RELY trial (Connolly et al N Engl J Med 2009; 361:1139-1151) with dabigatran vs warfarin) and 50% reduction in ICH. The Committee noted that, although there was a significant reduction in ICH in the equivalent rivaroxaban trial (ROCKET AF – Patel et al, N Engl J Med 2011; 365:883-891), there was no reduction in major bleeding when rivaroxaban was compared with warfarin. The Committee noted that apixaban also provides an option other than warfarin for those with ESRD who are at increased risk of bleeding and calciphylaxis, although this is retrospective data only at this stage.

6.19. The Committee noted that there are no head-to-head randomised controlled trials comparing DOACs for the prevention of stroke in those with AF. The Committee considered that the meta-analyses overall show that apixaban is the preferred agent for individuals at high risk of major bleeding, as it overall has the most favourable safety profile. The Committee considered that rivaroxaban appears to have the highest risk of bleeding, and that this is likely due to the once daily dosing resulting in a high peak concentration of the drug. The Committee noted that apixaban has a comparatively lower renal excretion of 25%. The Committee considered that apixaban provides a suitable alternative for those requiring anticoagulation treatment with a high risk of bleeding (including GI bleeding) and those with ESRD.

6.20. The Committee noted that idarucizumab, the reversal agent for dabigatran, is very effective and currently funded in New Zealand. The Committee noted that the only reversal agent commercially available for Factor Xa inhibitors (eg rivaroxaban and

apixaban), andexanet alfa, is not currently funded or Medsafe approved in New Zealand, this is also the case in many other jurisdictions, however it has recently been approved by the Therapeutic Goods Administration (TGA) in Australia (June 2022). The Committee noted that, in the absence of dedicated reversal agents for Xa inhibitors, prothrombin complex concentrate or factor eight inhibitor bypassing activity products (FEIBA) are used in the event of severe bleeding. The Committee therefore considered that a specific reversal agent is not required prior to funding of apixaban and noted that this was not a requirement prior to funding of rivaroxaban.

Suitability

6.21. The Committee noted that dabigatran is available as an oral capsule which cannot be chewed, broken, or opened as this may increase the bioavailability of dabigatran (PRADAXA Medsafe datasheet. DOR Mar 2020). The Committee noted that rivaroxaban and apixaban are oral tablets which can be crushed and mixed with water or other bases and administered orally for those who unable to take tablets, or mixed with a small amount of water and administered via a gastric tube (XARELTO Medsafe datasheet. DOR May 2021; ELIQUIS Medsafe datasheet. DOR Aug 2019). The Committee considered that rivaroxaban and apixaban are therefore more suitable options for children, or those with swallowing difficulties, which is commonly the case for people who have had a stroke who require treatment with anticoagulants.

6.22. The Committee considered that, if apixaban were to be funded, support would be required to educate healthcare professionals on the implementation of treatments. The Committee considered that there are no known groups that could not reasonably be transitioned between DOAC agents or to a generic DOAC. The Committee considered three months to be a reasonable period to transition individuals to alternate agent brands.

Cost and savings

6.23. The Committee considered that it would be appropriate to include DOACs in the Pharmac annual Invitation to Tender (ITT), a competitive procurement process run annually for some medicines and related products. The Committee additionally considered that it would be clinically appropriate to fund generic versions of dabigatran, rivaroxaban and apixaban.

6.24. The Committee considered that, if apixaban were to be funded, health sector expenditure on hospital admissions associated with anticoagulant-related bleeding events would potentially decrease due to a reduced risk of this adverse effect occurring on apixaban, compared to other anti-coagulants. The Committee considered that anticoagulation-related bleeding events often require the administration of reversal agents (for dabigatran) and intensive monitoring, which are both highly resource intensive.

6.25. The Committee considered that, if apixaban were to be funded, open listing would be preferred. The Committee considered that if Special Authority criteria are required, it would be appropriate to target use to those considered to be at high risk of life-threatening bleeding, or bleeding which would threaten critical organ function. The Committee considered it would be appropriate to include those requiring stroke thrombolysis.

Discussion

6.26. The Committee noted that the health need for people with haemophilia is still being addressed by the haemophilia treatments contracted for as a result of the competitive process in run in 2018, and that the contracts for these products had been extended to June 2024. The Committee noted that while the end of the sole supply period is June 2024 the products concerned will continue to be supplied past that date.

6.27. The Committee noted that the relevant historical framework for haemophilia treatments has been supported by Pharmac since 2013, with access to treatments currently managed by the Haemophilia Treaters Group (HTG) and the National Haemophilia Management Group (NHMG). The Committee noted that access to emicizumab however is enabled via Special Authority.

6.28. The Committee noted that the 2018 Request for Proposal (RFP) resulted in the introduction of Extended Half Life (EHL) product categories for both Factor VIII (FVIII) and Factor IX (FIX), as well as the provision of Rare Clinical Circumstances (RCC) brands which made provision for the use of legacy funded products where a transition to the Preferred Brand was deemed clinically problematic.

6.29. The Committee noted that the transition of people from the Short Half Life (SHL) products to the Extended Half Life (EHL) products for both Haemophilia A and B had occurred fairly rapidly with a high level of acceptance by those taking the products.

6.30. The Committee noted that current FVIII and FIX usage is now likely at a steady state following the trend over the last few years to increase target trough levels to enable better bleed control.

Haemophilia A

6.31. The Committee noted that the majority of people with severe Haemophilia A are currently on FVIII prophylaxis.

6.32. The Committee noted that there are two EHL FVIII products approved by Medsafe, with another product under review and another which has TGA approval. The Committee noted that there are six SHL FVIII products with Medsafe approval.

6.33. The Committee considered that transitioning people to a new agent is a significant undertaking, and is resource intensive, so a reasonable time needs to be allowed for a transition period in any brand change process.

6.34. The Committee considered that a six-month transition period would be appropriate should there be the need to transition to another Factor VIII product as a result of any competitive process. The Committee considered that this would be manageable within the current treatment framework and would adequately minimise any associated clinical impact.

6.35. The Committee noted that some of the FVIII EHL products have longer half-lives than others which may allow the maintenance of higher trough levels, which may translate to better bleed control or facilitate longer time between infusions.

6.36. The Committee Considered that there was only a clinical need for one SHL FVIII and one EHL FVIII product, but that it might be possible to have only an EHL FVIII product as individuals could use either SHL or EHL product in an ‘on demand’ treatment approach.

6.37. The Committee considered that clinically, it would be appropriate to have only an EHL FVIII product, as individuals treated 'on demand' could use either SHL or EHL products. However, the Committee considered that for those few individuals for whom a SHL product may be required, it would be important to enable access to a SHL product. The Committee noted that a small number of individuals have been reluctant to transition to the pegylated EHL FVIII products due to the theoretical issue of the development of inhibitory antibodies against polyethylene glycol (PEG) and perhaps PEG accumulation with long-term use. The Committee however considered that the 5% Alternative Treatment Allowance (ABA) would be sufficient to facilitate the use of SHL FVIII if only an EHL FVIII product was contracted to service the FVIII market.

6.38. The Committee noted that it would be important to engage with other haemophilia bodies such as the Haemophilia Treaters Group (HTG), the Haemophilia Foundation and the National Haemophilia Management Group (NHMG) regarding the intent and structure of a new haemophilia commercial process.

6.39. The Committee noted that the uptake of emicizumab by individuals with haemophilia A who have FVIII inhibitors had been rapid and there were now 17 people receiving emicizumab across the country.

6.40. The Committee noted that there is research ((Bukkems et al, Thrombosis and Haemostatis 2022 Feb; 122 (2): 208-215)) into using a whole vial dosing approach with regard to emicizumab whereby dose by weight is rounded to the closest vial size presentation to reduce wastage. The consequent period between doses can then be adjusted to ensure therapeutic efficacy is retained.

6.41. The Committee noted that if emicizumab was to be funded for all severe haemophilia A patients a single SHL FVIII would be the only other FVIII product required to treat those receiving 'on-demand' treatment.

6.42. The Committee noted that the use of emicizumab in children with severe haemophilia A would address a high health need by avoiding the requirement for the use of implanted ports to administer FVIII product. However, the Committee noted that creating a sub-group of people for funding consideration based on age was problematic and that an alternative criterion may be required which targets the specific need. It was noted that this issue had been discussed in previous meetings.

6.43. The Committee noted that once individuals had transitioned to emicizumab from an infusion-based treatment, if funded, it would be difficult to return to an infusion due to the ease of use of a subcutaneous treatment. The Committee considered that it should be achievable for people to transition to another subcutaneous therapeutic option should competitor products to emicizumab become available.

Haemophilia B

6.44. The Committee noted that there had been a strong uptake of EHL FIX product in those with haemophilia B, where the advantages of a reduced infusion schedule are significant, however there is still a reasonable level of residual SHL FIX use.

6.45. The Committee noted that there are currently two EHL FIX products which are Medsafe approved and an additional product which has TGA approval. The Committee also noted that there are two SHL FIX products with Medsafe approval.

6.46. The Committee noted that due to the lower level of use for FIX products stock control is more problematic and it would be helpful to be able focus treatment using fewer products and ideally limit use to a single EHL product, with no SHL product. The committee considered that people treated 'on-demand' could be treated with

only an EHL product, but that such a move would require a reasonable period of transition time clinically.

7. Therapeutic Group and NPPA Review

Overall Summary

7.1. The Committee noted the consistent growth in medicine costs for the group since the last review in particular the increased usage for direct oral anticoagulants (DOACS).

Expenditure Summary

7.2. The Committee noted that of the 15 agents with gross expenditures greater than $1M in the year ending 30 June 2022, that DOACS (dabigatran and rivaroxaban) dominated the spend closely followed by products used for the treatment of haemophilia. The Committee considered that the high prevalence of atrial fibrillation may contribute to the high DOAC use observed.

Named Patient Pharmaceutical (NPPA)

7.3. The Committee noted the number of NPPA requests received for the funding of eculizumab for the treatment of atypical haemolytic uremic syndrome (aHUS). The Committee considered that it would be appropriate to consider an application for this indication as eculizumab has become the standard of care for this condition overseas. The Committee also noted that eculizumab has a role in the treatment of transplant associated thrombotic microangiopathy (TATMA).

7.4. The Committee noted that there had been no NPPA applications for the use of eculizumab for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). The Committee considered that although PNH was a serious condition, only a small proportion of individuals with this condition would require treatment with a C3 complement inhibitor such as eculizumab.

Horizon Scan

7.5. The Committee considered a range of pharmaceutical agents that are currently in the late stages of clinical trials or have recently achieved regulatory approval and should be considered for future funding applications.

7.6. The Committee noted the development of concizumab, a novel subcutaneous prophylactic therapy for both haemophilia A and B. The Committee noted that concizumab is a haemostatic rebalancing agent that binds to the Kunitz-2 domain of tissue factor pathway inhibitor (TFPI). The Committee noted that concizumab has been reported in clinical trials to be capable of treating both haemophilia A and B with and without inhibitors.

7.7. The Committee noted the development of MIM8, which is a next generation bispecific FVIII mimetic for subcutaneous prophylaxis to treat individuals with haemophilia A with or without inhibitors, being developed by Novo Nordisk and is currently in Phase 3 trials. The current FRONTIER trials evaluating MIM8 are using monthly dosing to achieve effective treatment thresholds.

7.8. The Committee noted the recent developments in gene therapy for both haemophilia A and B, with etranacogene dezaparvovec for the treatment of haemophilia B likely to gain FDA approval in the near future. The Committee noted that gene therapy is likely to become the dominant treatment option, however noted that pricing of these agents may pose a significant issue with regard to affordability.

7.9. The Committee noted that sutimlimab a first-in-class humanised immunoglobulin G4 (IgG4) monoclonal antibody that selectively inhibits the classical complement pathway at C1s. It has been reported in the Cadenza study to be efficacious in the treatment of cold agglutinin disease (CAD), a rare haemolytic anaemia disease that has traditionally been treated with blood transfusions and other supportive care. The Committee noted that in the trial treatment with sutimlimab resulted in the avoidance of transfusion in 73% of patients in the treatment arm versus 15% of patients in the placebo arm.

7.10. The Committee noted that ciraparantang, a novel reversal agent for a range of anti-coagulants, is said to be progressing well in Phase 3 clinical trials. The Committee noted that ciraparantang can be used to reverse the effects of the DOACs dabigatran, rivaroxaban, edoxaban and apixaban, and can also be used as a reversal agent for enoxaparin. The Committee noted that currently the only funded DOAC with a reversal agent also funded is dabigatran with the agent idarucizumab. The Committee noted that anticoagulant-associated bleeding is a significant reason for emergency hospital admission, and considered in cases of life-threatening bleeds such as intracranial haemorrhage that the availability of a reversal agent would be beneficial. The Committee noted that andexanet alfa, the only available reversal agent for the use in conjunction with FXa inhibitors such as rivaroxaban, is very expensive and considered that if funded it would need to be restricted in its use to the treatment of life-threatening bleeds.

7.11. The Committee noted that there have been a number of developments in the treatment of immune thrombocytopenia (ITP), notably the agent rozanolixizumab, which is a subcutaneously administered, humanised monoclonal antibody that specifically binds, with high affinity, to human neonatal Fc receptor (FcRn). It has been designed to block the interaction of FcRn and Immunoglobulin G (IgG), accelerating the catabolism of antibodies and reducing the concentration of pathogenic IgG autoantibodies.

7.12. The Committee noted that imatinib, a tyrosine kinase inhibitor funded initially for the treatment of gastrointestinal stromal tumours (GIST) and now open listed for other treatments, has also shown encouraging results in the treatment of ITP. The Committee also noted that another Bruton's tyrosine kinase inhibitor (BTK) inhibitor, rilzabrutinib, has had reported utility as a 3rd line therapy for refractory ITP (Kuter et al , N Engl J Med. 2022 Apr 14;386(15).)

7.13. The Committee noted that the use of eltrombopag has increased following a decision to widen access for use in idiopathic thrombocytopenic purpura and severe aplastic anaemia in 2018. The Committee considered it likely that demand had now peaked following this change in Special Authority criteria.

7.14. The Committee considered that the majority of people likely to transition from short half-life (SHL) FVIII products to extended half-life (EHL) FVIII products would have already done so. The Committee considered that the remaining SHL FVIII usage was likely due to more aggressive treatment in the on-demand setting and in order to achieve higher trough levels of FVIII in those remaining on SHL based prophylaxis. The Committee considered that apart from small increases in utilisation per person there is unlikely to be any systematic significant increase in FVIII usage in the next few years.

7.15. The Committee noted that FIX SHL product use was still relatively high given that the FIX EHL product has considerable benefit in terms of reduced infusion requirement. The Committee considered that this is possibly due to its use in individuals with mild and moderate haemophilia B who are being treated with on demand infusions.

7.16. The Committee noted that with the declining use of the FIX SHL products that it is becoming harder to manage stock to avoid expiration and subsequent wastage. The Committee noted that coordinating stock between different treatment centres has proved to be difficult.

7.17. The Committee noted the significant impact of the introduction of emicizumab for people with severe haemophilia A with inhibitors on the use of the FVIII bypassing agent factor VIII bypassing activity (FEIBA). The Committee noted that given the reduced demand for FEIBA, the management of stock had become a significant issue as there remains a need for this agent for emergency use.

7.18. The Committee noted that FVII (NovoSeven) usage has been relatively static over the past 5 years, as it is used in special circumstances, such as when a person taking emicizumab undergoes major surgery. The Committee noted that there are other FVII products commercially available internationally, including a biosimilar to NovoSeven (eptacog alfa) and two recently commercialised eptacog beta products which have demonstrated similar utility to eptacog alfa in clinical trials.

7.19. The Committee noted that there may be concerns from those using pegylated products over the longer term and the potential for anti-PEG immune response, should there be only an EHL product available for prophylaxis of Haemophilia A and B.

7.20. The Committee noted that in terms of future procurement there would not be a clinical requirement to have a rare-clinical circumstances brand as part of a commercial process, as people had effectively transitioned to EHL products following the previous competitive process.

7.21. The Committee noted that PTAC had considered an application for the use of ticagrelor for the treatment of minor stroke in August 2022 and recommended it for funding with a low priority, and that the Cardiovascular Advisory Committee in June 2022 had considered a clinician application for the relisting of prasugrel based on new information from the ISAR REACT 5 trial reporting clinical outcomes more favourable than that for ticagrelor, which was recommended with a high priority.

7.22. The Committee noted that there had been steady growth in the use of enoxaparin sodium over the past 5 years. Members considered that the primary reason for this was likely to be due to increased use for VTE prophylaxis in cancer treatment, particularly for colorectal cancer surgery, and as a preferred prophylaxis option over aspirin for orthopaedic surgery.

7.23. The Committee noted that no tender award for the supply of enoxaparin sodium was made following a recent Invitation to Tender process, due to concerns raised regarding suitability and support for the disposal of needles in the community. The Committee noted that there is currently considerable variation in the availability of dedicated sharps containers across New Zealand and that in many situations it is acceptable for alternative household containers to be utilised.

7.24. The Committee noted the growth in the use of blood colony stimulating factor agents over the past five years. The Committee noted that the increase in the use of pegfilgrastim was attributed to the widening of access in April 2020, which lowered the febrile neutropenia risk requirement criterion from 20% to 5%. The Committee noted that this change was implemented in response to the effects on the health sector of the Covid-19 pandemic and national response. It was noted that, subsequent to a tender award, a brand change for pegfilgrastim will take place early in 2023; the Committee considered that this would be unlikely to create any issues and didn't believe any specific brand change activities would be required.

7.25. The Committee noted the continued decline in the use of warfarin and the consequential growth in the use of DOACS (dabigatran and rivaroxaban).

8. Desmopressin Acetate DDAVP - To increase the FVIII concentration in people with Haemophilia A, von Willebrand disease or inherited platelet disorders

Application

8.1. The Committee reviewed the application seeking listing of desmopressin acetate (DDAVP) 15 mcg/mL vial in the community (currently only listed in HML), submitted on behalf of the National Haemophilia Treaters Group by a member of the Haematology Advisory Committee.

8.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

8.3. The Committee **recommended** that desmopressin acetate (DDAVP) 15mcg/mL vial be funded in the community for management of acute bleeding or prophylaxis for minor surgery in people with moderate and mild Haemophilia A, von Willebrand Disease or inherited platelet disorders with a **high** priority, within the context of haematology treatments.

8.4. In making this recommendation, the Committee considered that listing this product for community use would provide meaningful benefits to those living with the above conditions by improving the ease of access and timeliness of desmopressin treatment.

Discussion

Māori impact

8.5. The Committee considered that the unmet need in relation to the impact of mild to moderate Haemophilia A, von Willebrand disease or inherited platelet disorders on Māori health outcomes was similar to that of non-Māori in terms of ease of access to treatment.

Need

8.6. The Committee considered that this application aimed to target people with:

- Haemophilia A (predominantly mild, also a small proportion of individuals with moderate haemophilia A) or haemophilia A carriers; and especially those with high-risk mutations who would benefit from avoiding factor VIII [FVIII] exposure where possible.
- Mild von Willebrand disease, predominantly type I without a von Willebrand Factor [VWF] gene variant, but also some people with type II (not IIB or III)
- A small proportion of people with clinically impactful, nonspecific, bleeding disorders (eg including some inherited platelet disorders).

8.7. The Committee noted that the type of bleed that has occurred (eg mild muscle bleeds or epistaxis, not joint bleeds) and/or the type of low-risk surgery planned (eg dental procedure or skin lesion removal or biopsy) determines the approach to

management . The Committee noted that more significant bleeds or surgeries would require the use of FVIII or FVIII with von Willebrand's factor (Biostate).

8.8. The Committee noted that treatment protocols including desmopressin are developed according to an individual's need and procedure or bleed type, taking into account baseline FVIII level and the desired FVIII response (typically at least 30%) and duration. The Committee noted that current best practice is for these individuals to receive an initial dose of desmopressin under the supervision of a haematologist to identify those who benefit, given variable responses are anticipated due to factors including von Willebrand genotype and FVIII levels.

8.9. The Committee noted that von Willebrand disease prevalence in New Zealand is approximately 0.01% based on the current literature and real-world experience in Auckland. The Committee noted that in Auckland there are about 160 people with von Willebrand disease (mostly type I), 178 with mild haemophilia A, 10 haemophilia A carriers, and a small number of individuals with nonspecific bleeding disorders. The Committee noted that in Auckland in the previous 12 months, 10 people with von Willebrand disease and two individuals with mild haemophilia A received desmopressin for minor surgery and muscle bleeds, respectively.

8.10. The Committee noted that the majority of people with mild haemophilia A or von Willebrand disease currently receive desmopressin in a hospital setting alongside their treatment protocol and are well known to their closest haemophilia treatment centre. However, the Committee considered that there are differences in access in different parts of the country and in some regions individuals need to travel several hours to attend their closest centre.

8.11. The Committee considered that the health need in this population resulted from the challenges in accessing this formulation of desmopressin in a timely manner for offsite use, predominantly for minor surgical procedures and minor bleeding issues which do not require blood products. The Committee considered that the unmet need in relation to the impact of mild to moderate Haemophilia A, von Willebrand disease or inherited platelet disorders on Māori health outcomes was similar to that of non-Māori in terms of ease of access to treatment.

Health Benefit

8.12. The Committee noted that desmopressin is a synthetic form of the normal human hormone arginine vasopressin (the antidiuretic hormone, or ADH) which mimics the FVIII stress response and increases vWF/VIII levels. The Committee noted that a number of desmopressin presentations are already funded for community and hospital use without restriction and that the requested presentation (15mcg/mL vial; Octostim brand) is listed in Section H.

8.13. The Committee noted that that DDAVP 15mcg/mL vial Octostim) is approved by Medsafe for the therapeutic control of bleeding and bleeding prophylaxis in connection with minor surgical procedures in those with mild haemophilia A and von Willebrand's disease who respond positively to a test dose (although must not be used in von Willebrand's disease type IIB).

8.14. The Committee noted that the application recommends desmopressin acetate (DDAVP) 15mcg/mL vial be used at a dose of 0.3 mcg per kg subcutaneously (SC) for acute bleeding (either a single dose or with a second dose 12 hours later if required), or prophylaxis (a single dose prior to a surgical procedure with one or two doses postoperatively if required). Members considered that this reflected the dosing used for standard of care in New Zealand and noted that the maximum volume administered would be up to 2.0 mL with a response expected to peak in about two

or three hours. The Committee considered that there is extensive clinical experience with desmopressin in New Zealand for bleeding disorders and that it is often used in combination with tranexamic acid.

8.15. The Committee noted that the submission included six publications providing evidence and guidelines regarding the use of desmopressin in this context, and that Pharmac staff identified three additional publications of relevance:

- Kadir et al. Fertil Steril. 2005;84:1352-9
- Loomans et al. Haematologica. 2018;103:550-7
- Mannucci P M. Treatment of Haemophilia. 2012;11
- Mannucci P M. Haemophilia. 2000;6 Suppl 1:60-7
- Trigg et al. Haemophilia. 2012;18:25-33
- Hews-Girard et al. Haemophilia. 2018;24:720-5
- Karanth et al. Cochrane Database Syst Rev. 2019;2:CD009824
- Sreeraman et al. Thromb Res. 2022;213:16-26
- Akin M. Hematology. 2013;18:115-8

8.16. The Committee considered that funding the 15mcg/mL vial in the community would not be expected to reduce FVIII usage due to the mild phenotype seen in those affected. The Committee considered there might be a small reduction in hospital visits where telephone management occurs instead.

8.17. The Committee noted that desmopressin doses are limited to avoid tachyphylaxis (ie only one or two doses over 48 hours), that the risks of fluid retention and occasional severe hyponatraemia are managed with a cautious approach for the very young and the elderly (eg with vascular disease), that people with nonspecific bleeding disorders and normal or high FVIII levels may develop very high FVIII levels leading to an increased thrombotic risk, and that risks associated with intravenous fluids would not be expected with minor surgery or minor bleeds. The Committee considered that the known risks would not increase substantially if the 15mcg/mL vial were funded in the community, as current practice involves an initial trial dose to determine response, careful management, and age selection.

8.18. The Committee considered that clinical use of desmopressin would not be expected to increase significantly if the 15mcg/mL vial were funded in the community, and it would continue to not be used for all bleeding events (eg not for unexplained perioperative bleeds, and not for severe haemophilia A or von Willebrand disease types IIB or III where little benefit would be expected). The Committee considered that desmopressin would unlikely be used as a primary treatment for individuals with mild bleeding or menorrhagia although a small proportion of those so affected would be diagnosed with von Willebrand disease and therefore use desmopressin in later lines after tranexamic acid and other treatments.

8.19. The Committee considered there would likely be a small increase in the total use of desmopressin if it were to be funded in the community, as some people who live further away from a hospital currently go without treatment for some milder bleeding events. The Committee considered that these individuals would be expected to receive desmopressin if it were to be funded in the community. The Committee considered that this would represent a minority of individuals, and that the majority of community desmopressin use would be among those who are currently receiving it in a hospital setting.

Suitability

8.20. The Committee considered that the key benefits of funding desmopressin 15mcg/mL vial in the community would be improved ease of access and earlier access to treatment, which might prevent ongoing bleeds and be especially beneficial for those individuals who live at a distance from their haemophilia treatment centre. The Committee considered that those known to respond to desmopressin could also avoid an additional visit to their haemophilia treatment centre and could receive desmopressin in the community either prior to, other treatments (if needed), or instead of receiving treatment in hospital. The Committee further considered this would enable them to access minor surgery in the community with minimal risk and would be useful for those who may need to or wish to travel (eg for work or recreation).

8.21. The Committee considered that funding the 15mcg/mL vial for community use would not pose challenges in terms of subcutaneous administration given that many people living with haemophilia and their caregivers are familiar with the technique. The Committee considered it could also be used easily by primary care nurses, or in private hospitals, with support from the haemophilia treatment centre regarding dosing, timing and management of side effects. The Committee noted that appropriate disposal of the syringe and sharps would be required.

Costs and Savings

8.22. The Committee considered that funding the 15mcg/mL vial for community use would not significantly change desmopressin use overall due to current practice. However, the Committee noted that a dispensing fee would be applied at point of collection.

8.23. The Committee considered that most individuals who would switch to using desmopressin 15mcg/mL vial in the community would previously have been receiving this in hospital, although most of these individuals would not have received FVIII or Biostate given the mild disease phenotype of the target population.

8.24. The Committee considered that the usage of combination therapy with desmopressin and FVIII (eg for significant procedures) would be unchanged, and therefore that a reduction in FVIII usage would not be expected and overall treatment cost would likely be unchanged.

Special Authority criteria

8.25. The Committee considered that specific funding criteria was not required given the appropriate and careful use of current treatments, including treatment protocols, for this population group.

Summary for Assessment

8.26. The Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for desmopressin acetate (DDAVP) 15mcg/mL vial if it were to be funded in New Zealand for the community management of acute bleeding or prophylaxis for minor surgery in people with moderate and mild Haemophilia A, von Willebrand Disease or nonspecific bleeding disorders. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and

may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	People with mild haemophilia A without inhibitors Small proportion of individuals with moderate haemophilia A assumed to use desmopressin Some haemophilia A carriers	People with von Willebrand disease who respond well to an initial dose People with clinically impactful, nonspecific, bleeding disorders (eg including some inherited platelet disorders)
Intervention	Desmopressin acetate DDAVP 0.3mcg/kg administered to either treat bleeds, or as prophylaxis prior to minor surgery or dental procedure. 1-2 repeat doses may be required.	
Comparator(s) (NZ context)	Either: a) Desmopressin in a hospital setting, OR b) Small proportion of individuals with mild bleeds who are currently going without treatment	
Outcome(s)	Reduced requirement for travel to hospital (ie easier and more timely access to treatment) Small increase in the number of bleeds being treated (which is likely associated with health-related quality of life improvements)	

9. Ferric Carboxymaltose - Use in patients with serum ferritin of 20mcg/L to 50mcg/L and C-reactive Protein (CRP) > 5 (P-001566)

Application

9.1. The Advisory Committee reviewed a clinician-initiated application for widened access to ferric carboxymaltose for the treatment of anaemia and chronic inflammatory disease.

9.2. The Advisory Committee noted that Pharmac sought advice from the Haematology Advisory Committee regarding the proposed Special Authority criteria following PTAC's review of this application in February 2022.

Recommendation

9.3. The Advisory Committee **recommended** that access to ferric carboxymaltose in the community be widened for the treatment of iron-deficiency anaemia with chronic inflammatory disease with a **high** priority, subject to the following Special Authority criteria (changes in **bold** and ~~strikethrough~~):

Special Authority for Subsidy
Initial application – (serum ferritin less than or equal to 20 mcg/L, or 20 to 50 mcg/L in **chronic inflammatory disease**) from any relevant practitioner. Approval valid for 3 months for applications meeting the following criteria:
Both:

1. Patient has been diagnosed with ~~iron-deficiency~~ anaemia; and
    - 1.1. Serum ferritin level is less than or equal to 20 mcg/L; or
    - 1.2. Both:
        - 1.2.1. Serum ferritin is between 20 and 50 mcg/L and
        - 1.2.2. C-Reactive Protein (CRP) is ≥5 mg/L; and

2. Any of the following:
    2.1. oral iron treatment has proven ineffective; or has resulted in dose-limiting intolerance; or
    2.3. Rapid Correction of anaemia is required.

Renewal – (serum ferritin less than or equal to 20 mcg/L, or 20 to 50 mcg/L in **chronic inflammatory disease**) from any relevant practitioner. Approval valid for 3 months for applications meeting the following criteria:
Both:

1. Patient continues to have iron-deficiency anaemia with a serum ferritin level of less than or equal to 20 mcg/L **or between 20 and 50 mcg/L with CRP of ≥5 mg/L**; and
2. A re-trial with oral iron is clinically inappropriate.

9.4. The Committee considered that administration in a community setting was preferable for people with iron deficiency and chronic inflammation and was desirable to address current inequity of access, as there was significant pressure on New Zealand's infusion services and access would be enhanced for those individuals residing more rurally or in smaller centres.

9.5. The Committee noted that it can be difficult to accurately diagnose iron-deficient anaemia using laboratory tests (including complete blood count (CBC) as there were no clear definitions for the condition. The Committee considered that the serum ferritin levels included in the proposed Special Authority criteria would not always indicate that someone was anaemic, however on balance the Committee considered that the serum ferritin level as specified would be clinically acceptable, as requiring additional criteria using haemoglobin thresholds would be unnecessarily restrictive in the community setting.

9.6. The Committee noted that the proposed C-reactive protein threshold in the Special Authority of 5 mg/L was at the upper end of the normal range and would be a relatively low value on which to define a significant inflammatory condition.

9.7. The Committee noted that there was a potential risk that by widening ferric carboxymaltose access to this expanded group of individuals in a community setting, as the potential existed for the inappropriate diagnosis and treatment of anaemic disorders.

9.8. The Committee considered that widening access to ferric carboxymaltose in the community for this population group would be unlikely to have a significant impact on the overall numbers of people treated. The Committee considered that most people being treated for iron deficient anaemia and chronic inflammatory disease would already be receiving access to ferric carboxymaltose in the secondary care setting.

9.9. The Committee noted that the risk of anaphylaxis associated with iron infusion with ferric carboxymaltose was very low but that community-based infusion providers have management plans in place to deal with such events.