Record of the Reproductive and Sexual Health Advisory Committee Meeting held on 13 March 2025

Reproductive and Sexual Health Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

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

The Reproductive and Sexual Health 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
Elizabeth Dennett (Chair)
Helen Paterson
Julie Avery
Martin Wilson
Rhiannon Braund
Ruth Swarbrick
Christine Pihema
Beth Messenger

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Liraglutide for the treatment of weight gain associated with polycystic ovarian syndrome in women with insulin resistance	Decline
• Drospirenone and ethinylestradiol (20 microgram) within the context of treatments for reproductive and sexual health	High priority
• Drospirenone and ethinylestradiol (30 microgram) within the context of treatments for reproductive and sexual health	Medium priority
• Lidocaine with prilocaine within the context of treatments for reproductive and sexual health, if lidocaine for prilocaine for IUD insertion was available on a Practitioner Supply Order (PSO)	High priority

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

3.1. This meeting record of the Reproductive and Sexual Health Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.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 6.4 of the SAC Terms of Reference.

3.3. The Reproductive and Sexual Health Advisory Committee is a Specialist Advisory Committee of Pharmac. The Reproductive and Sexual Health Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Reproductive and Sexual Health Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Reproductive and Sexual Health 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 Reproductive and Sexual Health that differ from the Reproductive and Sexual Health 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 Reproductive and Sexual Health Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Reproductive and Sexual Health.

4. Welcome and introduction

4.1. The Committee was welcomed with a karakia followed by whakawhanaungatanga.

4.2. The Chair acknowledged the passing of Dr Stella Milsom. Dr Milson joined Pharmac as a member of the previously named Hormone and Contraceptive Subcommittee of PTAC in 2009 and went on to become a member of the Endocrinology Advisory Committee. Dr Milson was a pioneering endocrinologist and made a lasting impact through her work for Pharmac and for Sexual Reproductive Health in New Zealand.

5. Record of previous Reproductive and Sexual Health Advisory Committee meeting held Monday, July 18, 2022

5.1. The Committee reviewed and accepted the record of the Reproductive and Sexual Health Advisory Committee held 18 July 2022.

6. Pharmac Update

6.1. The Committee noted the Pharmac Update.

7. Therapeutic Group and NPPA Review

Discussion

Hormonal Contraceptives

7.1. The Committee noted that the current Special Authority criteria for some oral contraceptives require a discussion related to the patient's income. The Committee considered this to no longer be appropriate for the purposes of targeting access to funded treatment and supported removal of this criteria, noting that there is a lack of awareness around the existence of it as it stands, and it is therefore rarely used with limited to nil impact on current access.

7.2. The Committee considered that having more funded options for hormonal contraceptives will better serve the population. The Committee considered this to be supported by the significant uptake of any given product in this therapeutic group when it is funded.

7.3. The Committee also noted that issues in supply such as shortages can only be expected to worsen, given the current international supply chain and influences on it. There are no contraceptives produced in New Zealand, so supply is dependent upon imported products. The Committee considered that having more funded options available will help to protect against a situation where choices are greatly diminished due to issues in supply.

7.4. The Committee considered that 12-month prescriptions of hormonal contraceptives should become standard in future to increase access.

7.5. The Committee discussed recent research on reproductive coercion and identified that Women's Refuge had completed work in this space. Members identified that ethnic groups such as Indian people may require further support and research in future.

<u>Ethinylestradiol with levonorgestrel</u>

7.6. The Committee noted that due to supply issues and the absence of a suitable replacement, Pharmac was considering the option of replacing the 30 microgram ethinylestradiol with 150 microgram levonorgestrel combined pack containing seven inert tablets, with a pack that does not contain the seven inert tablets.

7.7. The Committee noted that it is usual practice for prescribers to advise people to skip the inert tablets in an oral contraceptive pack.

7.8. The Committee noted that combined oral contraceptive products are based on a 28-day cycle, including inert tablets, and most individuals will receive a three- or six-month supply per prescription. The Committee considered that many individuals will take active tablets continuously, with some taking a four-day break when necessary (eg in cases of breakthrough bleeding). The Committee noted that those people using active tablets continuously need to receive prescriptions more often if the inert tablets are counted in the number of tablets dispensed.

Medroxyprogesterone acetate

7.9. The Committee considered that a subcutaneous (SC) formulation of medroxyprogesterone acetate (Depo-SUBQ provera) would be advantageous and may support equitable access to appropriate contraceptive treatments, given that it can be self-administered.

7.9.1. The Committee noted that there are clinics charging high fees for administration of medroxyprogesterone acetate intramuscular (IM) injection and this is a financial barrier to certain populations. The Committee was made aware of data which show Māori and Pacific wāhine to be the highest users of medroxyprogesterone acetate (Depo-Provera), along with those living in areas of high socioeconomic deprivation.

7.9.2. The Committee considered that there are a number of examples of injected pharmaceuticals that are self-administered, showing that this is an acceptable approach for many people. The Committee considered that self-administration also supports contraceptive autonomy. The Committee considered it important to note that a significant proportion of the New Zealand population are not enrolled with a General Practitioner (GP) or cannot easily access a GP.

7.9.3. The Committee considered that the sense of control with a self-administered presentation may be very acceptable to certain groups, including those who feel long-acting reversible contraceptives (LARCs) result in a loss of contraceptive autonomy.

7.9.4. The Committee considered it difficult to predict the number of individuals who would move from an IM to a SC presentation of medroxyprogesterone acetate if it were to be funded. The Committee noted that there are a number of individuals who do not like to self-administer and would prefer to receive the three-monthly IM injection administered by a trained healthcare professional.

Emergency Contraceptives

Ulipristal acetate

7.10. The Committee considered that there is an unmet need within the context of oral emergency contraception, due to the limited efficacy window of the currently funded option following unprotected intercourse. The Committee considered this need could be addressed by funding ulipristal acetate, which is widely available internationally and has demonstrated efficacy.

7.11. The Committee noted that although an application was submitted to Pharmac, there is no Medsafe approved ulipristal product for emergency contraception which prevents the funding application from being progressed. This is in accordance with Pharmac policy, where medicines funding applications can only be progressed once the medicine has been submitted to, or approved by, Medsafe.

7.11.1. The Committee noted that there are some exceptions where some medicines are funded without Medsafe approval and are available via Section 29 (S29). However, the Committee considered that this is not practical for the provision of contraceptives as it is very restrictive and presents significant barriers to prescribers and patients (such as prescribing nurses and pharmacists being unable to prescribe S29 medicines).

Funded emergency contraception

7.12. The Committee considered that there is evidence that the levonorgestrel emergency contraceptive is less effective in those weighing over 70 kilograms (kg) and that more than 50% of individuals with a potential for pregnancy have weight greater than this. The Committee noted that there is evidence to support that doubling the dose of levonorgestrel does not impact the efficacy for people with a body mass index (BMI) over 30mmKg^2, where a single dose is shown to be less effective. (Edelman et al. Obstet Gynecol. 2022; 140(1):48-54).

7.12.1. The Committee noted that Māori and Pacific populations are statistically more likely to weigh more than 70 kg a trend influenced by both genetic and sociocultural factors. Given that the efficacy of certain oral emergency contraceptives decreases with increasing body weight, this represents a significant area of potential health inequity. The Committee considered it to be extremely important to ensure equitable access to emergency contraceptive options that maintain clinical effectiveness across a range of body weights. The Committee considered that addressing this disparity would improve reproductive health outcomes (eg abortion rates, unwanted pregnancy continuations, and morbidity and mortality rates) for priority populations.

7.13. The Committee considered that insertion of an intrauterine device (IUD) is a form of emergency contraception that is able to be used up to five days after unprotected intercourse, but that access to insertion is a barrier. The Committee considered there to be two effective solutions to this issue, which require healthcare practitioner support, given the devices are available on Practitioners' Supply Order (PSO), and these solutions are:

7.13.1. Improving intra-uterine device (IUD) training and so they can be accessed in the necessary time frames

7.13.2. Practitioners to recognise and use the 52 mg levonorgestrel IUD (Mirena) as an emergency contraceptive

7.14. The Committee were made aware that if there is no use of contraception, then there are eighty-five unintended/unplanned pregnancies in a year in New Zealand per 100 sexually active people of childbearing potential. This number is reduced to between thirteen and eighteen unintended/unplanned pregnancies per year if condoms are used and if effective emergency contraceptive is added to this, then the number of unintended/unplanned pregnancies would be further reduced down to approximately one to four pregnancies in a year. The Committee considered that this is not dissimilar to pregnancies associated with using a combined oral contraceptive, which is the most commonly prescribed contraceptive method.

Gynaecological anti-infectives

7.15. The Committee noted that Pharmac currently has a funding application for clindamycin vaginal cream (Dalacin V) for the treatment of desquamative inflammatory vaginosis, however, there is no Medsafe-approved vaginal cream product in New Zealand.

7.15.1. The Committee considered that a clindamycin vaginal gel would be an acceptable alternative for most people, but there may be people for whom the gel may not be suitable depending on the ingredients and potential allergens.

7.16. The Committee noted that dispensing data indicated that there was an increase in the use of clotrimazole in 2022 which could be explained by the change in prescribing practices due to an increase in the use of telehealth, as was seen with increased antibiotic prescribing during the COVID-19 pandemic.

7.17. The Committee considered that the moxifloxacin Special Authority criteria for treatment of mycoplasma genitalium (mGen) is onerous and does not meet its intent, which was to ensure appropriate prescribing. The Committee noted that it also acts as a barrier for certain institutions.

7.17.1. For example, Sexual Wellbeing Aotearoa clinics do not have access to funded mGen testing and permission must be requested from a sexual health physician. If the requirement for nucleic acid amplification test (NAAT)-confirmed mycoplasma genitalium was removed from the Special Authority, it would enable treatment of people who have persistent symptoms but a negative STI swab, who the Committee considered would likely benefit from moxifloxacin. However, the Committee considered that if the current Special Authority criteria were to be retained, then barriers to mGen testing should be removed.

Obstetric Preparations

Early medical abortion (EMA)

7.18. The Committee considered that a pre-prepared pack with the appropriate amounts of mifepristone/misoprostol required for early medical abortion (EMA) and clear instructions would have improved patient suitability compared with current practice, which is for healthcare providers to make up a combination pack using the individual medicines.

7.18.1. The Committee considered a pre-prepared combination pack would have better safety and be clinically beneficial, primarily by prevention of dosing errors.

7.19. The Committee considered that a pre-prepared combination pack would impact the use of misoprostol. The Committee considered that current practice is to give the patients ten misoprostol tablets even if they would not all be used, to avoid the patient having to travel back to collect more. The Committee considered that a pre-prepared pack would not displace the use of misoprostol for other indications such as induction of labour, preoperative use, or for miscarriage.

7.19.1. The Committee considered that approximately 90% of EMA usage would be transferred to the pre-prepared combination pack if it were funded in New Zealand.

7.20. The Committee noted previous clinical advice regarding the need for a lower dose misoprostol (25 microgram) for use in hospital in induction of labour and that current processes involve dissolving the 200 microgram tab in liquid solution and using a proportion of this. The Committee acknowledged there was uncertainty around supply of a feasible product in New Zealand, however considered it would offer a suitability benefit (reducing staff time) that may improve safety over the current method of dissolving the higher dose tablet in water and using an aliquot.

7.21. The Committee considered that the largest increases in rates of medical abortion have already occurred, although there will still be increasing use from miscarriage

cases. The Committee considered that as medical management of abortion becomes more integrated into primary care practice, and as awareness and accessibility improve, there is a potential for a broader range of healthcare practitioners – including nurses – to provide this care in diverse community settings. The Committee considered that these improvements in service delivery may support greater uptake and improve timely, community-based access, particularly for priority populations. Ensuring equitable access for Māori and Pacific peoples will be essential to addressing current disparities in reproductive healthcare.

7.22. The Committee noted that although both individual products (mifepristone and misoprostol) that would make up the combination pack for EMA are Medsafe registered, a specific Medsafe approval for the pre-prepared combination pack would be required as it would be considered a new product (taking into account factors such as manufacturing, safety, packaging etc).

Pregnancy Tests – hCG Urine test

7.23. The Committee considered that low sensitivity pregnancy tests are sent out with the misoprostol/mifepristone EMA care packages and that low sensitivity tests are only clinically appropriate in the context of early medical abortion.

7.24. The Committee noted that in an EMA, there is a 1-3% risk of the person still being pregnant following the procedure. The Committee noted that it takes time for hCG levels to decrease to levels less than what is detected by high sensitivity pregnancy tests. The Committee noted that the low sensitivity hCG test is appropriate for confirming the completion of the process.

7.25. The Committee considered that the availability of the high sensitivity pregnancy test on prescription would be particularly beneficial in a telehealth setting where the person would otherwise need to purchase a test. The Committee noted that most general practice clinics have high sensitivity pregnancy tests available on hand, and that there wouldn't be a significant increase in usage if they are made available on prescription but usage may shift from Practitioners Supply Order (PSO) to prescriptions.

7.25.1. The Committee considered that the funded pregnancy test kit lacks instructions, making it potentially unsuitable for use outside of the healthcare setting. However, this may not be a significant issue given that people may have become more familiar with self-testing after using COVID-19 rapid antigen tests.

7.25.2. The Committee noted that pregnancy tests available in the retail sector include midstream dipsticks, dipstick tests and cassette-based tests that require collection of urine in a cup for subsequent testing. The Committee considered that people of some cultures may not be happy with an in-stream test and may prefer to using a dipstick/cassette test, or some may prefer the assistance of a trained healthcare professional to reduce risk of user error.

<u>Long-Acting Reversible Contraceptives (LARCs)</u>

7.26. The Committee noted that there have been significant issues with the availability of non-hormonal IUDs in the last 12 months.

7.27. The Committee noted that there is a preference for choice with IUDs. The Committee noted that short IUDs (29.1mm length x 23.2mm) were frequently used recently, however, this may have been due to supply issues with the other sizes. The Committee noted that all non-hormonal IUDs only have a five-year efficacy. The Committee considered that the narrowest IUD (35.5mm x 19.6mm) may be preferred

due to ease of placement, however, that it can be difficult to remove and may be less efficacious compared with other sizes as there is less copper material.

7.28. The Committee considered that if only one option was to be made available, then the preference would be for the standard size IUD. However, the Committee noted that a smaller IUD may be needed when using hormonal treatments which make the uterus cavity smaller (when using copper IUDs, there will be a lesser risk of cavity issues compared to using hormonal IUDs as copper does not impact cavity size). Members considered that short IUDs might be associated with an increased risk of expulsion in individuals where this is not the optimal size.

Horizon Scanning

NuvaRing

7.29. The Committee considered that there is an unmet health need that could be met with a hormonal vaginal ring (NuvaRing). The Committee considered that the preference for this product may be supported by user experience whilst being overseas and/or the desire to use a non-oral combined contraceptive option.

7.29.1. The Committee considered the uptake of a hormonal vaginal ring would initially be low, with the need to self-insert being a barrier. The Committee noted that although it would not be representative of the New Zealand population, data from the United Kingdom would be reasonable to use as an initial estimate.

7.29.2. The Committee noted that people of certain cultures may find a hormonal vaginal ring less appropriate due to the requirement to self-insert the ring in the vaginal vault.

7.29.3. The Committee noted that it is left in for three weeks, follow by a week without, but it can be left in for four-weeks for anyone that wants to use it continuously.

Implanon NXT

7.30. The Committee considered that although Accident Compensation Corporation (ACC) data wasn't analysed, it is likely that funding Implanon NXT would reduce the costs associated with the removal of difficult to remove subdermal implants. The Committee noted that Jadelle has two rods and considered that this may add to the difficulty of both implant insertion and removal.

7.30.1. The Committee noted that, irrespective of ACC cover, there are barriers to accessing radiology where this is required for removal.

7.31. The Committee considered that Implanon NXT is likely to be easier to insert and to train health care professionals on, compared with Jadelle. Members considered that, although they have not considered the published evidence, anecdotally in clinical experience there is less breakthrough bleeding with Implanon NXT and therefore they would expect greater continuation rates than what is observed with Jadelle.

7.32. The Committee considered that over time, it is likely that Implanon NXT would be preferred over the currently funded option (Jadelle). The Committee noted that there is evidence to support lessened efficacy of Jadelle after four years of insertion in individuals with a higher BMI. The Committee considered that for this reason, removal after four years is recommended for some individuals using Jadelle, rather than the five years in the Medsafe indication.

7.32.1. The Committee noted that Implanon NXT can currently be accessed through Section 29, however, there are barriers for both the patient and the healthcare professional.

Review of NPPA Applications

7.33. The Committee noted that there were a relatively low number of Named Patient Pharmaceutical Assessment (NPPA) applications for treatments for reproductive and sexual health.

Additional Consideration - 2024/25 Annual Invitation to Tender

7.34. The Committee noted that testosterone undecanoate injection (250mg per ml) and progesterone capsules (100mg) were both included in the 2024/25 Annual Invitation to Tender. The Committee noted that Pharmac sought further advice in the context of a potential brand change for these markets.

Testosterone undecanoate injection 250 mg per ml

7.35. The Committee noted that testosterone undecanoate is relevant to the gender affirming care population, where a brand change could be impactful. The Committee considered that it would be important to seek advice from individuals who would use these products.

7.36. The Committee considered that there would be a preference for vials over ampules in terms of ease of use.

Progesterone Capsule 100mg

7.37. The Committee noted that Pharmac may consider funding a bioequivalent progesterone capsule.

7.38. The Committee considered that a change to a generic progesterone capsule product would not be expected to cause any specific health concerns. The Committee noted that breakthrough bleeding is common during use of progesterone and should not necessarily be attributed to a change in brand if the funded brand is changed.

7.39. The Committee noted the importance of the funded product being suitable for both oral and intravaginal use. The Committee noted that for the unregistered indication of prevention of pre-term labour, the capsules are typically administered intravaginally. The Committee considered that there are reports suggesting that the oral route may be as efficacious as intra-vaginal use, however, there is a lack of evidence supporting oral administration in this indication.

7.40. The Committee noted that for menopausal hormone therapy (MHT), dosing is variable and that many women use 200mg either cyclically or continuously. The Committee considered that funding the higher dose capsule would be useful and noted that higher doses are being used more frequently as guidance evolves.

8. Liraglutide for the treatment of weight gain related to polycystic ovarian syndrome (PCOS)

Application

8.1. The Committee reviewed the consumer application for liraglutide for the treatment of weight gain associated with polycystic ovarian syndrome (PCOS) in women with insulin resistance. The Committee considered that the application targeted women with PCOS with a body mass index (BMI) of 30 kg/m^2 or greater, who have experienced insufficient benefit from metformin treatment.

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 the application for liraglutide for the treatment of weight gain associated with PCOS in women with insulin resistance be **declined.**

8.4. In making this recommendation, the Committee considered that:

8.4.1. There was a lack of high-quality and applicable evidence on the treatment benefit of liraglutide specifically in people living with PCOS, including long term benefit and safety.

8.4.2. The surrogate biomarkers for an overweight population cannot be transferred to a population who are overweight with PCOS.

8.4.3. Diagnosis rates for PCOS are low, therefore even if more funded treatments were available, many people with PCOS would remain inappropriately undertreated due to underdiagnosis being a substantial barrier to healthcare. (The Committee noted, however, that low diagnosis rates in isolation would not be a sole reason to recommend declining what may otherwise be a beneficial treatment)

8.4.4. There was no evidence to support targeting women with PCOS as a subgroup of those who could be considered for liraglutide.

8.4.5. That the unmet health need would be better addressed at a population level by making treatments more available for people requiring weight management medications.

8.4.6. If further evidence were to become available to inform the impact of liraglutide on fertility, this may be a reason to review the use of liraglutide for PCOS again.

8.5. The Committee considered that the Endocrinology Advisory Committee should review the record of its discussion on this application, including comments regarding fertility impacts and endometrial cancer risks.

Discussion

Māori impact

8.6. The Committee discussed the impact of funding liraglutide for PCOS on Pharmac | Te Pātaka Whaioranga's Hauroa Arotahi | Māori health areas of focus and Māori health outcomes. The Committee considered that underdiagnosis and also undermanagement may be more frequent in Māori with PCOS than non-Māori with PCOS.

Populations with high health needs

8.7. The Committee discussed the health need(s) of people with PCOS among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 as priority populations.

8.7.1. The Committee considered that the incidence of PCOS is likely at the same rate across various population groups, but that Māori and Pacific would be overrepresented within the population with PCOS for whom weight loss would be beneficial.

8.7.2. The Committee was made aware of data (a thesis by C Thomas, 2025) suggesting that people living in socioeconomically deprived or rural areas, Māori, and Pacific peoples, are not accessing anti-androgen combined oral

contraceptives as much as people of other ethnicities and thus considered these groups might not be able to fully benefit from funding a treatment for PCOS.

Background

8.8. The Committee noted that liraglutide (brand name Victoza) is funded for people with type two diabetes mellitus (T2DM) who meet Special Authority criteria relating to risk factors for cardiovascular or renal complications of diabetes.

8.9. The Committee noted that the presentation of liraglutide identified in this application (brand name Saxenda) was the same drug as is currently funded for people with type two diabetes mellitus (T2DM), but the Medsafe approvals for the two brands differ by indication and dose (Victoza Data sheet; Saxenda Data sheet).

8.10. The Committee noted that a separate application to fund liraglutide (Saxenda) for people with a BMI of at least 55 kg/m2 (or a BMI of at least 50 kg/m2 for Māori or Pacific peoples) with high cardiovascular risk, without T2DM, has previously been considered by PTAC and the Diabetes Advisory Committee. The application was deferred pending additional information on health benefit in this group (refer to Pharmac's Application Tracker for detail).

8.10.1. The Committee noted that PTAC had reviewed the key evidence on the use of liraglutide for weight management from the phase III SCALE trial (Pi-Sunyer X et al. N Engl J Med. 2015;373:11-22 - SCALE Obesity and Prediabetes trial) in November 2022, at which time it considered that the clinical relevance of reported improvements was uncertain, as most outcomes were surrogates requiring extrapolation (PTAC, November 2022). PTAC had also considered that the efficacy of liraglutide without significant diet and lifestyle intervention was unclear, and noted the variable provision of those interventions across New Zealand.

Health need

8.11. The Committee noted that PCOS is the most common endocrine disorder in women of reproductive age, with a prevalence of between 10-13% (Teedle et al. J Clin Endocrinol Metab. 2023;108:2447-69). Members recalled seeing international evidence that suggested that the prevalence of PCOS was similar across different ethnic groups, and although data was lacking in the New Zealand population, the Committee considered that prevalence of PCOS was unlikely to meaningfully differ across ethnic groups in New Zealand.

8.12. The Committee noted that the prevalence of overweight and obesity was higher among populations with high health need, such as Māori, Pacific peoples and disabled peoples. The Committee considered that these groups may be overrepresented among the group with PCOS and excess weight, but a large proportion may have also experienced barriers to PCOS diagnosis and may not currently be treated or managed correctly for the condition. Members were made aware of an unpublished observational study in New Zealand that reported significantly lower use of combined ethinyl oestradiol 35 microgram/cyproterone acetate 2mg (which is indicated in the treatment of PCOS) in people living in socioeconomically deprived or rural areas, and in Māori and Pacific peoples compared with people of other ethnicities. Members considered lower utilisation may be an indicator of underdiagnosis of PCOS among these groups.

8.13. The Committee noted that people with PCOS may have diverse symptoms including irregular menstrual cycles, excessive hair growth and impaired fertility (Louwers et al. Ther Adv Reprod Health. 2020;14:2633494120911038). The Committee noted that

PCOS was also associated with an increased risk of complications such as excess weight gain, type 2 diabetes, dyslipidaemia, and cardiovascular disease (Best Practice Advocacy Centre New Zealand, Understanding polycystic ovary syndrome, 2008).

8.14. The Committee noted that the internationally-accepted diagnostic criteria for PCOS were the Rotterdam criteria, which defined the condition by the presence of at least two of the following: oligo-anovulation (irregular menstruation), hyperandrogenism, and polycystic ovaries (Teedle et al. J Clin Endocrinol Metab. 2023;108:2447-69). The Committee noted that a diagnosis of PCOS may require individuals to receive an ultrasound, which in New Zealand is not publicly funded in primary care. The Committee considered that various barriers to testing combined with low public awareness of the condition meant that many cases of PCOS in New Zealand were undiagnosed and therefore untreated. The Committee therefore considered that the size of the unmet health need could not be well defined.

8.15. The Committee considered that most women with PCOS would be managed by a Specialist General Practitioner (GP) or endocrinologist, with reproductive medicine specialists possibly involved in the management of fertility-related complications. The Committee noted that standard of care treatment for PCOS included lifestyle interventions (diet and physical activity), use of the combined oral contraceptive pill, treatment with metformin and cosmetic interventions to address excess hair growth. The Committee noted that cosmetic interventions are not publicly funded. The Committee noted the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome which recommended that glucagon-like peptide-1 (GLP-1) receptor agonists and orlistat be considered as an adjunct to lifestyle interventions and metformin for people with PCOS and excess weight. The Committee noted that all recommendations for liraglutide are for its use in combination with other approaches and with metformin (unless already trialled and not tolerated).

8.16. The Committee noted that testing for insulin resistance was not routine for people with PCOS, given the limited clinical relevance of the available insulin assays. The Committee considered that the results of such testing were unlikely to guide treatment decisions.

8.17. The Committee considered that the fertility-related complications of PCOS may impact on family, whānau and others because they were a barrier to family formation and many of the treatments for fertility-related conditions could have an impact on partners. The Committee considered that while some people experiencing PCOS-related fertility complications may be eligible for publicly funded in-vitro fertilisation (IVF), the funded duration of treatment was two cycles and if the individual wanted to receive further cycles of IVF, these would need to be privately funded. Members considered that there was emerging research investigating the potential to stimulate fertility by using GLP-1 agonists to reduce body weight.

8.18. The Committee considered that the therapeutic intent of weight loss in PCOS was to reduce the risk of cardiometabolic complications and improve the individual's testosterone level profile, the latter being associated with many of the symptoms and fertility-related manifestations of the condition. However, the Committee considered that the guidelines for weight management in PCOS mirrored the recommendations relevant to the general population. The Committee considered that, although the drivers of weight gain in PCOS were distinct from other types of overweight and obesity, these differences in pathophysiology were unlikely to be relevant to the choice of weight management treatment or the threshold at which to offer weight management interventions.

8.19. The Committee considered that there was currently no clear reason to differentiate PCOS-related weight gain from other types of excess weight and therefore no clear rationale to target funding for those with PCOS rather than the wider population requiring weight management. The Committee considered that the unmet health need would likely be met by funding an effective treatment for a wider weight management group.

Health benefit

8.20. The Committee noted the application proposed liraglutide be considered for women with PCOS with insulin resistance, however, that it was not relevant to consider the benefits of liraglutide specifically in those with insulin resistance given this is not tested routinely for.

8.21. The Committee noted that the proportion of participants with PCOS in the SCALE trial (reviewed by PTAC in November 2022) was unknown and there were no subgroup analyses from the trial to inform whether people with PCOS experienced a different treatment benefit from those without the condition. The Committee considered that it was uncertain how applicable the SCALE trial evidence is to people with PCOS, as the drivers of weight gain and insulin resistance in PCOS were distinct.

8.22. The Committee noted the following observational studies on the use of liraglutide for the treatment of weight gain related to PCOS:

8.22.1. Elkind-Hirsch et al. Fertil Steril. 2022 ;118:371-81. SAXAPCOS: A randomised placebo-controlled phase III study of 82 nondiabetic, premenopausal women aged 18 to 45 years, diagnosed with PCOS with a body mass index of at least 30 kg/m2. Participants received either liraglutide (3 mg, n=55) or placebo (n=27) for 32 weeks. The mean weight loss with liraglutide was 5.7% (±0.75) vs 1.4% (±1.09) with placebo (P=0.002).

8.22.2. Jensterle et al Hormones (Athens). 2015;14:81-90. A randomised controlled trial of 32 non-diabetic newly diagnosed PCOS patients with BMI ≥30 who received liraglutide 1.2 mg (n=17) or metformin 1000 mg BID (n=15) for 12 weeks. Statistically significant reductions in BMI, body weight, waist circumference and whole-body fat mass were reported in both treatment arms, without significant differences between therapeutic groups.

8.22.3. Sever et al.Eur J Endocrinol. 2014;170:451-9. Open label prospective study of 36 people with obesity and PCOS who were pre-treated with metformin for at least six months. Participants received either metformin 1000mg BID (n=14), liraglutide 1.2mg QD (n=11) or combined metformin and liraglutide (n=11) for 12 weeks. The largest decreases in body weight and BMI were with the combination followed by liraglutide, with smallest reductions in the metformin alone group (P<0.001 for all comparisons).

8.22.4. Frossing et al. Diabetes Obes Metab. 2018;20:215-18. A double-blind, placebo-controlled, randomised clinical trial of liraglutide 1.8 mg/day or placebo for 26 weeks in 72 people with BMI >25 kg/m2 and/or insulin resistance. Compared with placebo, body weight in those on liraglutide reduced by 5.2 kg (5.6%), liver fat content by 44%, visceral adipose tissue by 18%, and the prevalence of non-alcoholic fatty liver disease by two-thirds (all P <0.01).

8.23. The Committee considered that these studies were generally small but of varying sizes and of low to moderate quality. The Committee considered that key concerns with the evidence were the short duration, with the longest study being 32 weeks, and noted that there were relatively high discontinuation rates due to intolerable side effects, The Committee considered that improvements such as a decrease in testosterone, improved insulin resistance, and decrease in glucose were less relevant

if only on treatment for a short duration of six months. The Committee also considered that weight rebound (ie regaining all the weight lost whilst on treatment) after stopping treatment would likely also occur in PCOS, as had been reported in studies of people without PCOS (PTAC, November 2022). The Committee also noted that benefits identified above are often seen from long term weight loss rather than short term weight loss.

8.24. The Committee was made aware of Bo et al. BMC Womens Health. 2025;25:64, an indirect comparison network meta-analysis that assessed the comparative efficacy of pharmacological interventions for PCOS. The authors reported that combining standard treatment with GLP-1 receptor agonists, with combinations including liraglutide and metformin (four studies), effectively reduced total cholesterol and LDL-C in PCOS patients and improved insulin resistance and glucose metabolism. Members considered this did not indicate a reduction in adverse cardiovascular outcomes, but that the evidence was still evolving.

8.25. The Committee noted Ge et al. J Endocrinol Invest. 2022;45:261-73 and considered this meta-analysis to be the most relevant, including six randomised controlled trials of liraglutide with or without metformin in overweight or obese women with PCOS. The Committee considered that this reported similar effects, but with its primary endpoints being surrogate outcomes for unmeasurable longer-term outcomes. The Committee considered that the benefits on an individual level were not able to be determined from this evidence, nor could it confirm outcomes for the broader target population.

8.26. The Committee also noted the following evidence:

- Rasmussen et al. Front Endocrinol (Lausanne). 2014;5:140
- Morais et al. J Diabetes Complications. 2024;38:108834
- Niafar et al. Arch Gynecol Obstet. 2016;293:509-15
- Tian et al. Minerva Med. 2022;113:542-50
- Wang et al. Obes Rev. 2018;19:1424-45
- Goldberg et al. Obes Rev. 2024;25:e13704.

8.27. The Committee noted that there was minimal long-term safety data in those liraglutide users with PCOS and that the available short-term data indicated most adverse effects were gastrointestinal effects (eg nausea). The Committee noted that the data suggests a benefit of combined treatment with liraglutide plus metformin over liraglutide monotherapy. However, the Committee considered the side effects of treatment may be additive with combination therapy, potentially leading to a shorter duration of use and reducing the treatment benefit.

8.28. The Committee noted an absence of evidence regarding any potential health benefits of liraglutide on fertility in PCOS, which it considered was highly relevant in this context.

8.29. The Committee considered that overall, there was a lack of high-quality evidence to inform the magnitude of health benefit of using liraglutide for weight management in the setting of PCOS. Additionally, the Committee considered that targeting this group, as opposed to groups with a similar health need (eg with high BMI), does not appear to be well supported by the evidence. The Committee considered that, aside from cardiometabolic benefits, the weight loss induced by GLP-1 agonists may be beneficial in PCOS due to other biologically plausible benefits related to improvement

of testosterone profile, including increased fertility and reduced endometrial cancer risk. However, the Committee considered that there was a lack of evidence to support these benefits and that it would therefore be inappropriate to include these health outcomes in an assessment of liraglutide for PCOS.

Suitability

8.30. The Committee noted that liraglutide is administered daily through a prefilled disposable pen. The Committee considered this to be an important suitability consideration, as frequent injections may affect adherence to therapy.

8.31. The Committee considered that treatment with liraglutide would be long-term, given many of the likely cardiometabolic benefits of GLP-1 agonist treatment would be accrued over timescales spanning years. The Committee considered that the lifelong nature of treatment was an important suitability consideration, however, that further long term data would be needed to help support this.

Cost and savings

8.32. The Committee considered that if liraglutide were to be funded for PCOS, it would be used secondary to lifestyle management and metformin use, however, uptake would be limited by the low rates of diagnosis for the condition. The Committee considered that the location of liraglutide in the PCOS treatment paradigm should not depend on insulin resistance status due to the barriers to assessing this.

8.33. The Committee considered that if liraglutide were to be funded for PCOS, this could increase public awareness of the condition and consequently the number of diagnostic investigations undertaken for PCOS. Members considered that some individuals might also seek investigation for PCOS with the aim of accessing liraglutide for weight loss. The Committee considered however that the cost to an individual for an ultrasound scan would remain a barrier to diagnosis and access.

8.34. The Committee noted that excess weight and insulin resistance are associated with a range of complications, which may result in costs to health sector budgets. The Committee considered that improved weight management and control of cardiometabolic risk factors among women with PCOS could result in savings to the health sector.

8.35. The Committee considered that, because of the uncertain treatment effect of liraglutide in the specific setting of PCOS, the magnitude and materiality of any health sector savings were highly uncertain.

General

8.36. Members considered that ensuring sufficient supply of liraglutide for people with diabetes was of key importance, and that funding it for additional indications would be inappropriate in the context of inadequate supply for people with diabetes.

Summary for assessment

8.37. The Committee considered that the PICO (population, intervention, comparator, outcomes) for this application was highly uncertain, with a lack of high-quality clinical evidence available to inform the outcomes of interest.

9. Drospirenone and ethinylestradiol (Yasmin and Yaz) for oral contraception, with or without treatment of moderate acne vulgaris or premenstrual dysphoric disorder (PMDD)

Application

9.1. The Committee reviewed the consumer application, and subsequent supporting application from Bayer Australia Limited, for drospirenone and ethinylestradiol (Yaz and Yasmin) for oral contraception and/or treatment of moderate acne vulgaris and/or premenstrual dysphoric disorder (PMDD).

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

Recommendation

9.3. The Committee **recommended** that drospirenone and ethinylestradiol (20 microgram) be listed with a **high priority** within the context of treatments for reproductive and sexual health.

9.4. In making this recommendation, the Committee considered the following:

9.4.1. The need for a range of contraceptive products, including combined oral contraceptives (COCs) with 20 microgram ethinylestradiol.

9.4.2. The potential for an additional benefit of drospirenone and ethinylestradiol (20 microgram) in the treatment of acne vulgaris and premenopausal dysphoric disorder (PMDD), although this is uncertain and might be a small difference compared with currently funded COCs.

9.4.3. Drospirenone and ethinylestradiol (20 microgram) is at least non-inferior to currently funded COCs in terms of contraceptive efficacy.

9.4.4. The safety profile of drospirenone and ethinylestradiol (20 microgram) compared with currently funded COCs that are used in the treatment of acne in particular, the risk of venous thromboembolism (VTE).

9.5. The Committee **recommended** that drospirenone and ethinylestradiol (30 microgram) be listed with a **medium priority** within the context of treatments for reproductive and sexual health.

9.6. In making this recommendation, the Committee considered the following:

9.6.1. The need for a range of contraceptive products, including combined oral contraceptives (COCs) with varying formulations.

9.6.2. Drospirenone and ethinylestradiol (30 microgram) is at least non-inferior to currently funded COCs in terms of contraceptive efficacy.

9.6.3. The safety profile of drospirenone and ethinylestradiol (30 microgram) compared with currently funded COCs that are used in the treatment of acne in terms of the risk of venous thrombosis (VT).

Discussion

Māori impact

9.7. The Committee discussed the impact of funding drospirenone and ethinylestradiol (30 microgram or 20 microgram) for contraception and considered the impact on Pharmac's Hauora Arotahi | Māori health areas of focus and Māori health outcomes. The Committee noted that Māori women are approximately 7% less likely to use

COCs than NZ European women. This difference may be due to Māori women having reduced access to primary health care services.

Populations with high health needs

9.8. The Committee discussed the health need of contraception among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of funding drospirenone and ethinylestradiol (30 microgram or 20 microgram) and noted:

9.8.1. Women living in areas of high socioeconomic deprivation have markedly reduced access to COCs compared to their less socioeconomically deprived counterparts.

9.8.2. In comparison to NZ European women, Middle Eastern/Latin American/African (MELAA) women have a COC usage rate ~8% lower, Asian women have a COC usage rate ~11% lower, and Pasifika women have a COC usage rate ~12% lower. However, this may be due to differential access to health care services, particularly reproductive and sexual health in NZ.

Background

9.9. The Committee noted that the Reproductive and Sexual Health Advisory Committee previously commented on the safety of ethinylestradiol with drospirinone in November 2021. At that time, the Subcommittee noted that ethinylestradiol with drospirenone had been Medsafe approved in New Zealand for some time, and Medsafe had considered that there were safety concerns with this medicine regarding the risk of venous thromboembolism.

Health need

9.10. The Committee noted access to contraception is a practice of human rights as it enables the individual to maintain health and gain control of their fertility.

9.11. The Committee was made aware of the Thomas et al. Aust N Z J Obstet Gynaecol. 2023 Jun;63(3):441-447 cross-sectional study assessing disparities in COC use in New Zealand. The study reported an inversely associated relationship between COC usage and socioeconomic deprivation, where people living in the least-deprived areas had approximately twice the usage rate of people living in the most deprived areas (17.01% and 9.4%, respectively). Inequity in COC use was also observed in terms of ethnicity, with 18.7% of NZ European females using COC, 11.88% of Māori females, 10.63% of MELAA females, 7.33% of Asian females, and 5.99% of Pacific females. The Committee considered that this recent evidence reiterated that access to, and prescribing of, contraceptives is suboptimal for several priority population groups.

9.12. The Committee was made aware of the increasing global burden of acne in adolescents and young adults, with the exception of New Zealand (Zhu et al. Br J Dermatol. 2025 Jan 24;192(2):228-237). The Committee noted a New Zealand study undertaken in 1998 reported an incidence rate of acne of 79% in females aged 16-18 years, with 1% of cases reported as severe (Pearl et al. NZMJ. 1998 Jul 24;111(1070):269-71). The Committee considered these were reasonable figures to apply at this time, however, that acne incidence in New Zealand may be underreported due to barriers in access to dermatology specialists. The Committee also considered that other currently funded oral contraceptive pills may provide a preventative effect in the treatment of acne in females.

9.13. The Committee was made aware of the Reilly et al. J Affect Disord. 2024 Mar 15;349:534-540 meta-analysis of premenstrual dysphoric disorder (PMDD) reported a

community based confirmed or provisional diagnosis prevalence rate a pooled sample of 50,659 participants. Overall confirmed diagnosis prevalence was 3.2% [95%CI 1.7%, 5.9%], and provisional diagnosis prevalence was reported at 7.7% (95%CI 5.3%, 11.0%). The Committee considered that a diagnosis of PMDD can be hard to obtain where there are strict diagnostic criteria. The Committee also noted a premenstrual syndrome (PMS) prevalence rate of 5-8%, in which many women also experience PMDD (Yonkers et al. Lancet. 2008 Apr 5;371:9619:1200-10).

9.14. The Committee considered that contraception is not a 'one-size fits all' and noted the need for a range of appropriate contraception methods, including oral contraceptives with different formulations. The Committee noted that there are currently six COCs funded in New Zealand. The Committee, however, considered that there are few distinct options, given that some COCs have the same active ingredients but there are a different number of active and inert tablets in each dispensed pack i.e. sugar or place holder pills compared with active pills.

9.15. The Committee considered that some people will take oral contraceptive pills continuously and without the sugar pill, will run out of medication sooner than those that take all pills dispensed.

9.16. The Committee noted that there is a large private market for drospirenone and ethinylestradiol and additionally, that there is very high funded use of ethinylestradiol and cyproterone compared with other countries.

Health benefit

9.17. The Committee noted that Yaz (drospirenone and ethinylestradiol (30 microgram)) is indicated in the treatment of PMDD and acne vulgaris, as well as for contraception while Yasmin (drospirenone and ethinylestradiol (20 microgram)) is indicated for contraceptive use only.

9.18. The Committee noted the following key clinical trials of drospirenone 3 mg and ethinylestradiol 30 microgram (Yasmin) for contraceptive efficacy, with the key outcome being the number of contraceptive failures per 100 women-years of exposure, i.e., the Pearl Index (PI):

9.18.1. Foidart et al. Eur J Contracept Reprod Health Care. 2000;5:124-34. A multicentre, open-label, randomised study (n=887) investigating the efficacy of Yasmin in comparison with a COC containing desogestrel and ethinylestradiol over the course of 26 menstrual cycles. The reported pearl index (PI) for both groups was 0.41 (adjusted PI = 0.0) which means that Yasmin has a comparable efficacy to a COC containing desogestrel and ethinylestradiol.

9.18.2. Huber et al. Eur J Contracept Reprod Health Care 2000;5:25-34. A randomised, open-label study (n=2069) investigating the efficacy of Yasmin in comparison with a COC containing desogestrel and ethinylestradiol over the course of 13 menstrual cycles. The reported PI in the treatment group was 0.71 (adjusted PI = 0.07), and 0.28 (adjusted PI = 0.28) in the comparison group.

9.18.3. Parsey and Pong. Contraception. 2000;61:105-11. An open label, multicentre study (n=326) investigating the efficacy and safety of Yasmin over 13 menstrual cycles. The study reported a PI of 0.406 (corrected PI = 0.407).

9.19. The Committee noted the following key clinical trials which reviewed the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram (Yaz) for contraception:

9.19.1. Bachmann et al. Contraception, 2004;70:191-8. An open-label, multicentre, non-comparative study that investigated the efficacy and safety of Yaz in 1049

participants over a period of 13 menstrual cycles. The reported uncorrected PI was 1.29 (upper limit of the 95%CI; 2.30) and the adjusted PI was 0.72 (upper limit of the 95%CI; 1.69) based on a total of 9010 treatment cycles.

9.19.2. Hernádi et al. Contraception, 2009;80:18-24. An open-label, uncontrolled, non-comparative, multicentre study reporting on the efficacy and safety of Yaz in 1129 participants. The study was conducted over a period of 13 menstrual cycles. The reported uncorrected PI was 0.49 (upper two-sided 95%CI of 1.14) and the corrected PI was 0.22 (upper two-sided 95%CI of 0.80).

9.19.3. Anttila et al. Contraception. 2009;80:445-51. A randomized, open-label, parallel group comparison study investigating the efficacy of Yaz compared to a COC with desogestrel in a participant group of 449 females over 7 cycles. There were no pregnancies reported in the treatment group and a PI of 0 (upper two-sided 95%CI of 3.4 and 3.55 for the uncorrected and corrected PI values, respectively).

9.20. The Committee noted the following evidence for the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram (Yaz) for acne:

9.20.1. Koltun et al. Contraception 2008:77:249-56 A randomized, double-blind, placebo-controlled trial that investigated the efficacy of Yaz in the treatment of acne vulgaris. The study reported an odds ratio (OR) of 4.31 [95%CI 2.11, 9.60] for 'clear' or 'almost clear' skin for the treatment group (n = 266) relative to the placebo group (n = 268).

9.20.2. Maloney et al. J Drugs Dermatol. 2009:8:837-44. A randomized controlled trial reporting on the efficacy of Yaz for the treatment of acne vulgaris. The trial reported decreased lesion counts, numbers of papules, pustules, nodules and open and closed comedones in the treatment group (n = 270) compared to the placebo group (n = 268).

9.21. The Committee noted that there is limited evidence on the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram for the treatment of acne. The Committee noted that the two trials had low participant numbers and were of relatively short duration (six cycles equating to 6 months). The Committee noted that the trials reported similar efficacy in skin improvement and that treatment was well tolerated. The Committee considered that the effects of the intervention (if measured by an odds ratio) would have been smaller if trialled in comparison with a COC, and that it is uncertain how the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram compares to other COC's in the treatment of acne. The Committee considered that the lack of active comparators in the evidence and the short duration of trials means the results need to be interpreted with caution.

9.22. The Committee noted the following primary evidence for the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram (Yaz) for PMDD:

9.22.1. Yonkers et al. Obstet Gynecol: 2005:106:492-501. A multicentre, double-blind, randomized clinical trial that investigated the efficacy of Yaz in the treatment of 450 participants with PMDD. The primary efficacy variable measured was difference between the average luteal phase Daily Record of Severity of Problems (DRSP) total scores from two pre-treatment qualification cycles and the average DRSP scores from three treatment cycles. The treatment group experienced a 47% reduction in the total DRSP scale from a mean (+/- standard deviation [SD]) of 77.40% (+/-16.7) during the two qualification cycles to an average of 41.2% (+/-17.3) for the three treatment cycles. The placebo group DRSP scores reduced 38%, from 78.1% (+/-17.8) to 48.1% (+/-21.2). Overall improvement using the Clinical Global Impression-Improvement observer-rated scale was greater for the treatment group

compared to the placebo group (2.2 vs. 2.5, adjusted mean difference was 0.30 [95%CI 0.55, 0.05; P=0.004 by rank ANOVA). Response, defined as a 50% decrease in daily symptom scores, occurred in 48% of the active-treatment group and 36% of the placebo group (relative risk 1.7, 95% CI 1.1 to 2.6; P = .015) and corresponds to a number-needed-to-treat of 8 patients.

9.22.2. The Committee noted that there was a significant improvement in the placebo group (38%) as well as the treatment group (48%). The Committee also noted the relatively short duration of the trial (two qualification visits and three treatment cycles).

9.23. The Committee also noted the following evidence for efficacy of drospirenone and ethinylestradiol (20 microgram) (Yaz) for PMDD:

- Pearlstein et al. Contraception. 2005:72:414-21
- Fu et al. Chinese J of Obstetrics and Gynaecology. 2014;49:506-9
- Eisenlohr-Moul. Depress Anxiety. 2017;34:908-17

9.24. The Committee considered that the body of evidence on the benefit of Yaz in the treatment of PMDD is insufficient in terms of health benefit, therefore the results need to be interpreted with caution. However, the Committee considered that the differences in outcomes between treatment arms would have been smaller if trialled in comparison with a COC, and that it is uncertain how the efficacy of drospirenone 3 mg and ethinylestradiol 20 microgram compares to other COCs in the treatment of PMDD.

9.25. The Committee noted the following evidence providing information on the safety of drospirenone and ethinylestradiol:

9.25.1. Ma et al. Cochrane. 2023 Jun 23;6:6:CD006586. A systematic review of randomized control trials comparing drospirenone and ethinylestradiol (20 microgram) with other COCs or placebo. The Committee noted that the review found that those taking COCs containing drospirenone and ethinylestradiol may be more likely to withdraw from trials due to minor adverse side effects (e.g. intermenstrual bleeding, nausea, and asthenia). The Committee noted that there were no serious adverse effects such as VT reported in trials. The Committee considered that COCs containing drospirenone and ethinylestradiol may contribute to improvement in productivity, social activities and relationships, as reported by DRSP scores, in comparison to placebo.

9.25.2. Dragoman et al., Int J Gynaecol Obstet. 2018 Jun;141(3):287-294. A meta-analysis of VT risk among users of COCs. The study analysed 22 studies and reported that users of drospirenone COCs had a VT risk ratio of 1.58 (95%CI 1.12, 2.14), lower than cyproterone 2.04 (95%CI 1.55, 2.49); desogestrel 1.83 (95%CI 1.55, 21.3), gestodene 1.67 (95%CI 1.32, 2.10). Dienogest and norgestimate had lower risk ratios of 1.46 (95%CI 0.57, 5.41) and 1.14 (95%CI 0.94, 1.32) respectively. Members considered that this study provided good evidence of the relationship between COCs and relative VT risk, noting there had been international speculation over past decades about VT risk relating more substantially to population factors instead.

9.26. Overall, the Committee considered that the evidence indicates that drospirenone and ethinylestradiol 20 microgram (Yaz) and drospirenone and ethinylestradiol 30 microgram (Yasmin) are likely to be as effective as currently funded COC in terms of contraception. The Committee considered it was uncertain whether outcomes for acne vulgaris or PMDD would differ with drospirenone and ethinylestradiol (20

microgram) compared with funded COCs based on the available evidence, however, any potential benefit over that of currently funded COCs for these outcomes would likely be small.

9.27. The Committee considered that people switching to a COC containing drospirenone may experience a reduction in the risk of VT incidence compared with currently funded acne medicines that are COCs.

Suitability

9.28. The Committee noted that COCs containing drospirenone and ethinylestradiol are packaged as either 21 or 24 active pills, with either seven or four inert (placebo or sugar) pills, respectively. The Committee considered that most COC users take the active pills only and that this is consistent with current prescribing advice.

Cost and savings

9.29. The Committee considered that many individuals may switch from currently funded COCs to a COC containing drospirenone and ethinylestradiol, particularly from COCs with higher VT risk such as cyproterone acetate with ethinylestradiol .

9.30. The Committee considered that if funded, drospirenone and ethinylestradiol may have high uptake from those initiating COCs for the first time although some clinical areas might not prescribe it for this initial use. However, the Committee considered that uptake from the relatively large private market for drospirenone and ethinylestradiol would contribute a large percentage of total uptake, and that overall uptake would increase slowly over time as awareness increases and prescribing patterns change.

Funding criteria

9.31. The Committee considered that drospirenone and ethinylestradiol (30 microgram and 20 microgram) should be open listed on the Pharmaceutical Schedule, to increase the number of available options and ensure people can access a COC that is suitable for them.

Summary for assessment

9.32. The Committee considered that the most appropriate focus for the proposal is contraception to prevent unintended pregnancies given the weak evidence of benefits for the treatment of acne and/or PMDD, which are uncertain compared with those from currently funded COCs.

9.33. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for drospirenone and ethinylestradiol (30 microgram or 20 microgram) if it were to be funded in New Zealand contraception. This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO table may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	This application considers the following indications 1. Contraception to prevent unintended pregnancies, particularly in those with acne or PMDD

Intervention	Drospirenone 3 mg & ethinylestradiol 20 microgram and drospirenone 3 mg & ethinylestradiol 30 microgram Active tablets are taken daily,
Comparator(s)	Other combined oral contraceptives include the following: • Ethinylestradiol with desogestrel • Ethinylestradiol with levonorgestrel • Ethinylestradiol with norethisterone • Cyproterone acetate with ethinylestradiol (relevant for acne) Active pills taken daily Pharmac staff note there is a relatively large existing private market in NZ for drospirenone and ethinylestradiol (30 microgram or 20 microgram) (Yasmin and Yaz) so the comparator for some will be 'no funded treatment' *Source: Community schedule, Contraceptives Hormonal*
Outcome(s)	***Contraception*** Yaz has comparable contraceptive efficacy and tolerability to the COC Marvelon (desogestrel 150 micrograms and ethinylestradiol 30 micrograms (21 tablets) and 7 inert tablets), and comparable bleeding and cycle control. Yasmin has comparable contraceptive efficacy compared to the COC Marvelon, and has comparable bleeding and cycle control. Yasmin's tolerability is comparable to other COCs. Yasmin has demonstrated improvements in body weight compared to Marvelon, and improvements in wellbeing and menstrual distress. ***Venous thromboembolism (VTE)*** Both Yaz and Yasmin: Reduction in DVT risk vs currently funded acne medicines that are COCs, for those who switch.
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

10. Lidocaine with prilocaine for the insertion of intrauterine devices (IUDs)

Application

10.1. The Committee reviewed the application for lidocaine with prilocaine for the insertion of intrauterine devices (IUDs).

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

Recommendation

10.3. The Committee **recommended** that lidocaine with prilocaine be listed with a **high priority**, within the context of treatments for reproductive and sexual health. This recommendation is only if lidocaine for prilocaine for IUD insertion was available on a Practitioner Supply Order (PSO).

10.4. In making this recommendation, the Committee considered that:

10.4.1. There is a health benefit from reduced IUD insertion pain, which is likely to improve uptake of IUDs; an effective form of contraception.

10.4.2. There would be improved equity in availability of lidocaine with prilocaine, therefore potentially providing a further contraception option for some living in high levels of socioeconomic deprivation.

Discussion

Māori impact

10.5. The Committee discussed the impact of funding lidocaine with prilocaine for insertion of IUD on Māori health areas of focus and Māori health outcomes. The Committee noted that there are structural barriers to accessing the person's contraceptive(s) of choice, including cost of services, distance from services, and wait times for appointments.

Populations with high health needs

10.6. The Committee discussed the health need(s) of funding lidocaine with prilocaine for the insertion of IUDs among Māori, Pacific peoples, disabled peoples including tāngata whaikaha Māori, and other populations identified by the Government Policy Statement on Health 2024-2027 to have high health needs. The Committee discussed the impact of funding lidocaine and prilocaine and considered:

10.6.1. The cost of contraception services, including IUD insertion, can be a barrier to individuals living in high levels of socioeconomic deprivation as measured by deprivation quintiles.

Background

10.7. The Committee noted that lidocaine with prilocaine cream for IUD insertion had previously been considered by the Committee in November 2021, who gave a positive recommendation, and that further advice was required following this recommendation on the health need of individuals and potential uptake of treatment.

10.8. The Committee noted that lidocaine with prilocaine cream is currently funded in the community for children with chronic medical conditions that require frequent injections or venepuncture, and is funded in hospitals without restriction.

Health need

10.9. The Committee considered that pain on insertion of an IUD is common although the magnitude of pain experienced by the individual is highly variable. The fear of insertion pain, or previous negative experiences, impacts people's decision on IUD use.

10.10. The Committee considered that there are limited options for pain management with IUD insertion. Current treatment includes paracetamol or ibuprofen 30 to 60 minutes prior to the procedure, however this is more effective for post-insertion pain rather than being used prior to insertion. There is some use of lidocaine 1% injection, however most clinicians are not trained in providing paracervical block, nor is it a part of the practice guidelines. There is also some use of lidocaine 2% gel, despite a lack of evidence supporting benefit.

10.11. The Committee noted recently updated US Selected Practice Recommendations for Contraceptive Use that recommended that all patients are counselled on potential pain during IUD placement, and that a person-centred plan be developed. The Committee considered that the approach and attitude of the clinician has an impact on the patient experience with IUD insertion.

10.12. The Committee considered that there is an equity issue in the availability of IUDs, with some people having them inserted through private clinics.

Health benefit

10.13. The Committee noted the evidence previously considered by the Committee in November 2021, along with updated Centers for Disease Control and Prevention (CDC) guidelines on contraceptive use, which incorporated evidence from three randomised controlled trials (RCTs) on lidocaine with prilocaine. The Committee noted that evidence indicates that lidocaine with prilocaine cream is effective at reducing IUD insertion pain. The Committee considered that lidocaine with prilocaine is likely to reduce distress for both the patient and their whānau or support person attending the procedure, along the anticipated procedure-related pain.

10.14. The Committee considered that effective pain management would increase uptake of IUD use, and that it may also reduce the number of IUD insertions that have failed.

10.15. The Committee considered that although the length of benefit from pain relief is for a short period (less than 30 minutes), there are long-term benefits from effective contraception.

10.16. The Committee considered that funding lidocaine with prilocaine cream will expand contraception options for individuals who might have avoided IUDs due to anticipated pain or distress.

Suitability

10.17. The Committee considered that lidocaine with prilocaine cream is easy to apply and therefore would be an option for any IUD insertor. It was noted that a paracervical block requires training.

10.18. The Committee noted that in various studies lidocaine with prilocaine cream was applied by the clinician, followed by the patient being required to wait 5-10 minutes for anaesthetic effect. This delay may make the procedure less suitable for both the clinician and patient. It may also increase insertion costs due to longer appointment times.

Cost and savings

10.19. The Committee considered the funding of lidocaine with prilocaine would have a small impact on use of lidocaine injection and lidocaine 2% gel, as these are only used in a small proportion of IUD insertions.

10.20. The Committee considered that uptake of lidocaine with prilocaine is difficult to assess as it is likely to vary across clinics and be dependent on factors such as the acceptance of the additional procedure time by both the clinician and patient. It is likely to be used in both first-time and subsequent IUD insertions.

10.21. The Committee considered that although there may be an increased cost of insertion due to longer length of procedure time, there may be savings from fewer failed first insertions, which would otherwise result in additional appointments and the cost of discarded IUDs.

10.22. The Committee considered that the funding of lidocaine with prilocaine cream is likely to increase IUD uptake among individuals who would have otherwise avoided this contraception option due to fear of pain or discomfort. However, it is unclear how many people would choose IUDs as a result of funding lidocaine with prilocaine cream, and which contraception options (if any) might be replaced as a result.

10.23. The Committee considered that one tube provides sufficient analgesic effect, and that there is unlikely to be cases where more than one tube is required. In most cases lidocaine with prilocaine cream would not be required for IUD removal.

Funding criteria

10.24. The Committee considered that treatment should be available to all IUD users without restriction to particular groups.

10.25. The Committee considered that there was also a need for pain management for endometrial sampling and stringless IUD removal. These procedures are increasingly undertaken in the community and cause pain similar to IUD insertion.

10.26. The Committee recommended that lidocaine with prilocaine cream be available Practitioner Supply Order (PSO). This would mean that an IUD pre-appointment would not be required, improving access to treatment. The Committee noted that if lidocaine with prilocaine cream was made available by PSO, it is highly likely to be used for clinical procedures beyond IUD insertion, as outlined on the Medsafe datasheet. In practice, the use for other indications could exceed use for IUD insertions.

10.27. The Committee recommended that lidocaine with prilocaine not be available on the Pharmaceutical Schedule under Special Authority criteria. The Committee noted that this would require individuals to have multiple appointments, creating barriers to access.

Summary for assessment

10.28. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for lidocaine with prilocaine if it were to be funded in New Zealand for insertion of IUD. This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO table may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	People receiving an IUD who need pain relief during insertion
Intervention	Lidocaine with prilocaine cream, 1x 5g (2ml) tube, applied 5-10 minutes prior to IUD insertion. Likely to be used in conjunction with standard non-topical non-localised pain relief, which is mainly aimed at alleviating post-IUD insertion pain unless the patient is allergic or these are contra-indicated for the person: • Non-steroidal anti-inflammatory drugs (NSAIDS) – Ibuprofen • Pain relief - Paracetamol
Comparator(s)	Majority of population: No treatment for IUD insertion pain A small proportion will receive lidocaine 1% injection for paracervical block or lidocaine 2% gel Will receive standard non-topical non-localised pain relief (unless the person is allergic or these are contra-indicated), which is mainly aimed at alleviating post-IUD insertion pain • NSAIDS – Ibuprofen • Pain relief - Paracetamol

Outcome(s)	**Reduced pain associated with IUD insertion** Compared to placebo, lidocaine with prilocaine statistically significantly reduced pain at tenaculum placement compared with placebo (mean difference −2.38; 95% confidence interval, −4.07 to −0.68. P<0.0001) (Samy et al. Fertil Steril. 2019: 111; 553-561). **Health-related quality of life (HRQOL) gains** HRQoL gains associated with pain reduction and reduced anxiety and distress around the procedure. **Increased uptake (and re-uptake) of IUDs** Increase in IUD uptake among sub-set of the eligible population who would have otherwise avoided this contraception option due to fear of pain or discomfort. Potential for **Changes in health system utilisation** • **Reduction in number of failed insertions** Failed insertions will result in additional appointments and unnecessary cost of discarded IUDs. Only a proportion of failed insertions will be due to pain/distress during insertion. • **Increase in IUD insertion procedure time** The intervention is applied pre-procedure and requires time to take effect, which may result in a longer procedure time.
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

11. Testosterone cream for the treatment of hypoactive sexual desire dysfunction (HSDD) in postmenopausal women – including review of November 2024 PTAC record

Application

11.1. The Committee reviewed a request from Pharmac staff to provide additional advice on the supplier application from Alchemy Health Limited for testosterone cream (AndroFeme 1) for the treatment of hypoactive sexual desire dysfunction (HSDD) in postmenopausal women and comment on the November 2024 record of PTAC's review of the application.

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

Discussion

Background

11.3. The Committee noted that from 1 April 2024, testosterone 16.2 mg/g transdermal gel (Testogel) was listed on the Pharmaceutical Schedule without restriction. This decision was the result of a Request for Proposals (RFP) by Pharmac for the supply of non-injectable testosterone. Testogel is indicated in adults as testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests (Testogel Medsafe Data Sheet).

11.4. The Committee noted that in November 2024, PTAC reviewed the application for testosterone 1% w/v cream (AndroFeme 1) for the treatment of hypoactive sexual desire dysfunction (HSDD) in postmenopausal women.

11.5. The Committee noted that PTAC had recommended the application to be declined and that in making this recommendation, PTAC had considered the following:

11.5.1. the uncertain diagnostic requirements for HSDD in post-menopausal women, potentially leading to inappropriate diagnosis and treatment, and noting a lack of clear clinical guidelines relevant to the New Zealand context

11.5.2. the eligibility criteria proposed as part of the application for AndroFeme 1 were not appropriate and posed significant barriers to equitable access for women, especially for some cultures who would not wish to undergo aspects of an HSDD diagnosis

11.5.3. the uncertain health benefit of AndroFeme 1 compared with funded testosterone gel (Testogel) [unapproved / off-label use]

11.5.4. the potential suitability issues in administering appropriate doses of Testogel for women, and a lack of data around the impact of this given the currently increasing use of Testogel by women

11.5.5. that the use of Testogel at equivalent mg dosages to AndroFeme 1 does not create a risk of supraphysiological levels of testosterone, given that the available pharmacokinetic data could not reasonably be generalised to suggest significant bioavailability differences between Testogel and AndroFeme 1 at equivalent milligram dosages

11.5.6. that there was poor understanding of long-term side effects due to a lack of evidence of the long-term use of testosterone in women. The Committee considered that potential virilising side effects from short term testosterone use can often be managed through appropriate treatment monitoring and adjustment.

11.6. The Committee noted that PTAC considered that Pharmac could seek further clinical advice, including advice from the Reproductive and Sexual Health Advisory Committee regarding their views on the application and PTAC's assessment.

General

11.7. The Committee noted that testosterone 16.2 mg/g transdermal gel (Testogel) is currently listed on the Pharmaceutical Schedule without restriction, which means that there is no fiscal barrier to limit its potential off-label use (i.e. outside its Medsafe approved indication). The Committee noted that prescribing data reports Testogel use by a large proportion of women, which is outside its Medsafe indication and therefore is unapproved or off-label use. The Committee noted that there is broad advocacy for testosterone therapy for women occurring currently on social media and considered that the magnitude of benefits portrayed in this setting may not align with those that would be expected at a population level based on the available evidence.

11.8. The Committee considered that the Testogel pump presentation, which dispenses a male-appropriate dose, means that many women who are using (or may seek to use) Testogel are likely to receive inappropriately high doses of testosterone that could result in potentially permanent adverse effects. Members considered that the method of aliquoting an appropriate dose for women (as described by PTAC) was not possible to do accurately, leading to excessive doses and that this was the main issue leading to concerns about the safety of Testogel when used by women. Members noted that it would be difficult to quantify this harm and considered that

Pharmac staff could obtain advice from endocrinologists who may manage patients who have experienced virilising adverse effects.

11.9. The Committee considered that due to the risk of permanent adverse effects, including permanent virilisation with high doses of testosterone in women, there is a need to consider funding a different testosterone product (such as AndroFeme 1) that would provide the dosage of testosterone required for women. However, the Committee considered that if it were not for this risk, there would not be a significant need to fund AndroFeme 1, or a different medicine, for this indication.

11.10. The Committee considered that AndroFeme 1 has clear suitability advantages compared to Testogel, with the ability to administer an appropriate dose of testosterone for women. Members considered that anecdotally, AndroFeme 1 use may lead to one additional pleasurable sexual experience per month and that this would likely be significant in the context of those experiencing less than this.

11.11. The Committee considered it was unreasonable to restrict funding of a different testosterone product with an appropriate dose for women (such as AndroFeme 1) to post-menopausal women with HSDD, given the numerous barriers to diagnosis and the fact that there would be women beyond this post-menopausal group seeking to access it (e.g. pre-menopausal women with HSDD).

11.12. The Committee considered that the number of women who would seek to be treated with a product such as AndroFeme 1 is unclear but could be substantial and considered that any future funding applications for women-specific testosterone products should describe this.

11.13. The Committee considered that if AndroFeme 1 was to be funded without restriction, many women would use it and all women currently receiving Testogel would be expected to take up AndroFeme 1 instead.

11.14. The Committee noted and agreed with PTAC's recommendation that testosterone 1% w/v cream (AndroFeme 1) for the treatment of hypoactive sexual desire dysfunction (HSDD) in postmenopausal women who meet the proposed Special Authority criteria be declined. However, the Committee considered that there is a need to provide a funded testosterone product that provides an appropriate dose for women to minimise the potential harm associated with off-label use of Testogel in women.