Record of the Mental Health Specialist Advisory Committee Meeting held on 4 February 2022

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

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

The Mental 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.

PTAC 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.

PTAC 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 PTAC 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

Alan Fraser (Chair)
David Chinn
Bronwyn Copeland
Jeremy McMinn
David Menkes
Giles Newton-Howes
Cathy Stephenson

Apologies:
Sean Hanna
Verity Humberstone

2. The role of PTAC Advisory Committees and records of meetings

2.1. This meeting record of the Mental Health Advisory Committee of PTAC is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Advisory Committees 2021, available on the Pharmac website at https://pharmac.govt.nz/about/expert-advice/specialist-advisory-committees/specialist-advisory-committee-terms-of-reference/.

2.2. The Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of PTAC Advisory Committees and PTAC.

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

2.4. The Mental Health Advisory Committee is an Advisory Committee of PTAC. The Mental Health Advisory Committee and PTAC and other PTAC Advisory Committees have complementary roles, expertise, experience, and perspectives. The Mental Health Advisory Committee and other PTAC Advisory Committees may therefore, at times, make recommendations for treatments for Mental 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 Mental Health that differ from the Mental Health

Advisory Committee, or PTAC Advisory Committees may make recommendations that differ from other PTAC Advisory Committees.

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

3. Correspondence and Matters Arising

Recommendations

3.1. The Committee **recommended** that the Special Authority for relevant ADHD medicines be updated to include diagnosis according to the DSM-5 or ICD-11 criteria.

Discussion

ADHD medicine access criteria

3.2. The Committee noted that current Pharmac Special Authority for Attention Deficit and Hyperactivity Disorder (ADHD), methylphenidate hydrochloride and dexamfetamine sulfate require diagnosis of ADHD according to the DSM-IV or ICD-10 criteria.

3.3. The Committee noted that the both the DSM-IV and ICD-10 criteria have been updated to the DSM-5 and ICD-11 criteria respectively. Members considered that these updated criteria have advantages over those previous and were in line with new evidence.

3.4. Members summarised that the main changes between the DSM-IV and DSM-5 criteria were:

- less barriers to ADHD diagnosis in adults, a reduction in hyperactive impulsive items from six to five.
- allowance for symptoms emerging later (change from seven years to 12 years of age).
- DSM-5 does not exclude people with autism spectrum disorder, as symptoms of both disorders can co-occur.

3.5. Members noted that the main update from ICD-10 and ICD-11 was the ‘grouping’ shift of ADHD from hyperkinetic disorders to neurodevelopmental disorders.

3.6. Members considered that, anecdotally, clinicians in New Zealand may use rating forms to inform ADHD diagnosis, when in practice these should be used only as a tool to trigger further investigation followed by assessment via formal criteria, ie. DSM or ICD to inform a diagnosis. Members considered that use of rating forms alone may lead to overdiagnosis.

3.7. Members discussed that there may be more advantages to using ICD over DSM, as it was developed to be universally applicable and does not reflect a singular American perspective. The Committee noted that in New Zealand, the DSM criteria are more commonly used to inform diagnosis than ICD, however that ICD was used for ‘diagnostic coding’. Members noted that it was not the place of Pharmac Special

Authority to alter clinical practice and considered it appropriate that the Special Authority continue to include both DSM and ICD diagnostic criteria.

3.8. Members considered it was likely that the DSM-5 criteria are currently used in practice in New Zealand rather than the DSM-IV and as such changing criteria to reflect the updated diagnosis was unlikely to abruptly result in an increased use of ADHD medicines.

3.9. The Committee noted that the new diagnostic criteria did lower the threshold for diagnosis of ADHD particularly in adults and that this may result in, over time, an increase in use of ADHD medicines. However, the Committee acknowledged that use of ADHD medicines continues to rise at a steady rate and that a change in required diagnostic criteria was unlikely to be the driving force behind any substantial change in medicine utilisation. Rather other factors, such as health sector resource would have a larger impact on use.

3.10. Members noted that currently, it is difficult to access specialists for ADHD assessment for patients (ie. with limited resources in secondary care) and that this presents a barrier to many individuals accessing treatments, given the treatments require specialist diagnosis and prescribing.

3.11. The Committee considered that moving forward it would be appropriate for Pharmac to update Special Authority criteria with updated diagnostic criteria as relevant.

Varenicline – vaping

Recommendations

3.12. The Committee deferred making a recommendation on widening access to varenicline for vaping cessation (in relation to both sole vaping and dual use). The Committee noted it would welcome a full funding application, with more detailed evidence to support the use of varenicline in this population.

Discussion

3.13. The Committee noted that varenicline was currently subject to a long term stock issue and not available at the time of consideration. The Committee noted that any changes, if relevant, to funding would occur following resolution of the stock issue.

3.14. The Committee noted that Pharmac had received a request for consideration of inclusion of nicotine vaping in the Special Authority criteria for varenicline. The Committee noted that currently, varenicline is only funded for patients who are attempting to quit “smoking” and meet other criteria.

3.15. The Committee considered that smoking rates in New Zealand appear to be declining, although that this trend is not observed in all groups - for example, lower socioeconomic status. The Committee considered that vaping is continuing to increase.

3.16. The Committee noted that currently nicotine replacement therapy and bupropion are fully funded without restriction and as such may be used in those with nicotine dependence who vape. The Committee considered that the patient cohort of those requiring nicotine dependency treatment from vaping was likely to be younger than

smokers and that in general, nicotine dependence disproportionately affects disadvantaged populations.

3.17. The Committee noted a cohort study investigating whether 'dual users' who smoke and use e-cigarettes were interested in using varenicline to stop smoking and if it was effective (Hajek et al. BMJ Open. 2019;9:doi:10.1136/bmjopen-2018-026642). The Committee noted that participants could opt to receive varenicline or not; of those who did receive varenicline, abstinence from smoking, vaping and dual use for at least 3 months was observed at a significantly higher rate than those who did not receive varenicline. The Committee noted that the abstinence rate was relatively low in both groups.

3.18. The Committee considered that the Hajek et al. study was of moderate strength. Members considered that given the mechanism of action of varenicline, it would be expected to be efficaious in the treatment of nicotine dependence from vaping. However, the Committee noted that there was limited data currently available to support the use of varenicline for vaping cessation.

3.19. Members considered that for a number of people who vape, the desire to quit vaping may not be as high compared to those who smoke (eg. it is seen as a 'healthier' option). As such, Members considered that it would be important to consider the role of selection bias in any assessment of evidence.

3.20. Members noted that evidence has shown that smoking cessation improves the rates of anxiety and depression (Taylor et al. BMJ. 2014; 348:g1151 doi: 10.1136/bmj.g1151). Members considered it would be interesting to explore if similar outcomes were observed with vaping cessation.

3.21. The Committee considered that widening of access to varenicline would result in a substantial increase in prescribing therefore a thorough consideration of the evidence should be conducted. The Committee noted it would welcome a full funding application.

3.22. The Committee noted that while varenicline can be very useful if used and followed up appropriately, varenicline can result in serious side effects, such as psychiatric symptoms, including psychosis (Medsafe. 2020). The Committee noted that because of this, varenicline treatment requires monitoring by the treating clinician which in a resource constrained health system may somewhat deter prescribing. As such, the Committee considered it important to thoroughly review evidence regarding widened access, noting that the clinical benefit to harm ratio was important to consider.

3.23. The Committee noted that Māori are disproportionately affected by smoking and vaping and as such it was important to maintain conversations regarding equity and smoking/vaping cessation treatments. Members considered that from an equity perspective, it was also particularly important to consider the potential side effects of varenicline, particularly psychosis.

3.24. Members considered that currently there is limited resource available to reduce smoking in New Zealand. Members considered that the availability of more / wider use of current pharmacological treatments would be a useful tool to assist in the reduction of smoking, although would need to be appropriately supported with other resources.

3.25. Members noted that the University of Otago was conducting research on rates of smoking, vaping, and dual use which would likely be useful to inform potential population size if this proposal were considered again in the future.

4. Therapeutic Group Review

Discussion

General

4.1. The Committee noted that since its last meeting PTAC had reviewed two funding applications for esketamine for treatment resistant depression and major depressive disorder with active suicidal ideation with intent. The Committee noted the record of PTAC's consideration and noted that PTAC recommended both of these applications be declined. The Committee considered that these recommendations were appropriate and did not consider that this Committee should review the full applications at this point in time.

4.2. Members considered that the 2009 recommendation of cost neutral for duloxetine remained appropriate. The Committee noted that this funding application had since been formally declined by Pharmac, however that this did not prevent reopening the application. The Committee considered that if the range of antidepressants available in New Zealand were to decrease, reconsideration should be given to this medicine.

4.3. The Committee noted the Named Patient Pharmaceutical Assessment (NPPA) applications received since its last meeting. The Committee noted that a large number of applications were withdrawn or did not meet the principles of NPPA. Members considered that further clinician education about the NPPA process may be beneficial. Members considered that the high bar and resource to make NPPA applications was a major barrier to clinicians applying for NPPA applications.

Horizon scanning

4.4. Members noted that trazodone is available overseas and used in the treatment of depression however Pharmac had not received a funding application to date. Members considered that there is a reasonably strong rationale for trazodone as a co-antidepressant, particularly in combination with selective serotonin reuptake inhibitors (SSRIs). Members considered that trazodone is a useful antidepressant and noted that it is sedating, compared with SSRIs which are alerting. The Committee noted that a small number of NPPA applications had been received for trazodone recently.

4.5. Members noted that brexpiprazole for treatment resistant psychosis was growing in popularity overseas.

4.6. Members noted that trifluoperazine, a typical antipsychotic, is available overseas however Pharmac had not received a funding application to date. Members considered that this medicine could supplement the range of funded antipsychotic agents in New Zealand. The Committee noted that a small number of NPPA applications had been received for trifluoperazine recently.

4.7. Members noted that guanfacine is used widely overseas for the treatment of ADHD and is a treatment of interest, however there is currently no approved product in New Zealand.

4.8. Members considered that pimavanserin for Parkinson's psychosis could add substantial value to the range of current treatments, particularly noting the side effects of currently funded alternatives for these patients. The Committee suggested that Pharmac staff explore opportunities for a funding application.

4.9. Members noted that an oral ketamine product was currently being developed for the treatment of depression. Members noted that the role of ketamine in the treatment of depression continues to be an area of research and development.

4.10. Members noted that a new monoclonal antibody, aducanumab was available overseas for the treatment of Alzheimer's disease, although its uptake internationally was sparse and sporadic. Members considered that the evidence of clinical benefit was disappointing to date, but that this drug would likely pave the way for more medicines in this area. Members considered that if such treatments were to be available in the future in New Zealand, the health sector impact should be considered, for example the availability of amyloid PET scans and biomarker tests.

Antipsychotics

4.11. The Committee noted that quetiapine use remained high and continues to increase. The Committee noted that quetiapine is often started for short term and off-label use, for example to aid sleep or a crisis episode. Members considered that it is likely over prescribed in primary care as people are continued on it following a crisis. The Committee noted that while quetiapine is a useful medication in certain circumstances, over a period of time it can result in serious side effects, including metabolic and cardiovascular impacts even when prescribed in low doses. As a result, long term use of quetiapine should be carefully considered and reviewed, with a focus on the risk-benefit profile for the individual patient and their circumstances. Members considered that educational information regarding managing and supporting patients in primary care could be useful to assist the appropriate use of quetiapine.

4.12. The Committee noted that the use of paliperidone continues to increase, while risperidone depot is decreasing. The Committee noted that both agents have the same active ingredient, however paliperidone has the advantage of monthly dosing compared with fortnightly. Members considered that the frequency of administration, together with effective marketing, was the likely driving force behind the change in use. The Committee considered that similar trends in use would continue to be observed, however that there would always be a population prescribed risperidone depot.

Anxiolytics

4.13. The Committee noted the high use of zopiclone compared with other funded hypnotics or anxiolytic agents. Members considered that the potential for abuse and dependency of zopiclone was somewhat lower compared with other funded agents in this group.

4.14. The Committee noted the high and increasing number of lorazepam prescriptions compared with other agents. Members noted that this may, at least to some extent be due safer prescribing of benzodiazepines (eg. more frequent prescribing) rather than increased units being dispensed. The Committee noted that in the future it would be most useful, particular for anxiolytics, to analyse volumes of

dispensed drug and patient numbers as opposed to the raw number of prescriptions.

Sedatives and hypnotics

Melatonin:

4.15. The Committee noted that melatonin use continues to be significantly higher than anticipated, with use continuing to increase. Members considered that use was likely to continue to increase in this manner under the current funding restrictions.

4.16. The Committee noted that the current Special Authority criteria allow a daily dose of up to 10 mg. The Committee noted it was not aware of any strong evidence to support use above 6 mg per day for those 18 years and under and considered it would be reasonable to consider a maximum daily dose restriction of 6 mg.

4.17. The Committee noted that in some overseas jurisdictions such as the USA, melatonin is classified as a dietary supplement and is readily available to consumers at a low cost. However in New Zealand melatonin is a prescription medicine, except when sold by a pharmacist for the treatment of primary insomnia for adults aged 55 years or older. Melatonin is only funded for individuals 18 years and under with insomnia secondary to a neurological disorder. The products available are relatively costly, either to the Schedule (if SA criteria are met) or to patients. The Committee suggested that Pharmac engage with Medsafe regarding the classification of melatonin and potential for a re-classification. Members considered that if melatonin were an over-the-counter medicine, it would likely improve access and could encourage competitive pricing.

Stimulants / ADHD treatments

4.18. The Committee noted that prescriptions for ADHD medicines continue to increase over time, particularly methylphenidate. The Committee considered that use would continue to increase at a similar rate, particularly given the current lack of nonpharmacological interventions/ support available in New Zealand.

4.19. The Committee noted that uptake of the Teva brand of methylphenidate extended release had not been substantial since its listing in November 2020, despite having a lower threshold of funding restrictions. Members considered that this was likely due to prescriber familiarity with the Concerta brand.

4.20. Members considered that the current ‘second line’ requirement for extended-release and modified-release methylphenidate (ie. immediate- or sustained-release used however ineffective due to administration difficulties or concern of diversion) was a relatively modest criterion and its removal would be unlikely to result in a substantial change in use.

4.21. The Committee considered that the need for stimulants should be reviewed regularly and discontinued when not conferring a significant benefit. Members considered that this may not routinely occurring in practice, in part due to current constraints on accessing specialist advice.

4.22. Members noted that due to the current barriers to specialist assessment, many primary care providers are initiating patients on atomoxetine and anticipate this will continue to increase. Members considered that education and support for primary care providers around the management of ADHD, including advice around

atomoxetine prescribing, the use of behavioural coaching, triaging for specialist assessment and activities which GPs can do to better manage these patients would be particularly helpful.

4.23. Members considered that wider availability of cognitive behavioural therapy, particularly for less severe cases of ADHD would likely have a large positive impact for patients.

Treatments for dementia

4.24. The Committee noted that the use of treatments for dementia has been relatively stable.

Treatments for substance dependence

Disulfiram

4.25. Members considered that the continued availability of fully funded disulfiram was imperative for those with alcohol use disorder, with no appropriate funded alternatives.

Varenicline

4.26. The Committee noted that varenicline is currently subject to a long-term supply issue and is not currently available. Members considered that there was minimal unmet health need as a result of this unavailability and that nicotine replacement therapy (NRT) was an appropriate funded alternative. Members considered however, that there did remain a place for varenicline in the funded treatment paradigm when supply resumes.

4.27. The Committee noted prior to this supply issue that use of varenicline had been decreasing. Members considered that this could be due to required monitoring when a patient is taking varenicline, compared with NRT.

Antidepressants

4.28. The Committee noted the importance of having a range of antidepressants with different mechanisms of action.

4.29. Members considered in particular that ongoing availability of an irreversible MAOI was important. The Committee noted that since phenelzine was discontinued, tranylcypromine is now the only funded irreversible MAOI antidepressant and as such its continued availability was imperative. Members noted that isocarboxazid is an alternative agent in this class and could be considered if required.

4.30. The Committee considered, with the exception of trazodone as discussed above, there was not a high need for any further funded agents, however noted it would be important to continually review the range of funded antidepressants, particularly if any further supplier-initiated discontinuations were to occur.

4.31. The Committee considered if supplier- initiated discontinuations were highly likely, or occurred in the future for any funded antidepressants it would be appropriate to restrict the agents to no new patients in order to target remaining stock to those already established on treatment.

5. Paliperidone three-monthly – schizophrenia

Application

5.1. The Advisory Committee reviewed a resubmission from Janssen for paliperidone three-monthly in the treatment of schizophrenia.

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

Recommendation

5.1. The Advisory Committee **recommended** that paliperidone three-monthly for the treatment of schizophrenia be listed with a **high priority** within the context of treatments in mental health, subject to the following Special Authority criteria:

> Initial application from any relevant practitioner. Approvals valid for 12 months for applications meeting the following criteria:
> All of the following:
> 1 The patient has had an initial Special Authority approval for paliperidone once-monthly depot injection; and
> 2 The patient has been diagnosed with schizophrenia (not another psychotic disorder); and
> 3 The patient has received at least four once-monthly paliperidone injections (excluding the additional initiation dose for patients who started on paliperidone once-monthly depot using the one-week initiation dosing regimen); and
> 4 At least the last two injections of paliperidone once-monthly injections were at the same dose; and
> 5 The patient has received clinical benefit from, and is considered to be clinically stable on, paliperidone once-monthly injections.
>
> Renewal from any relevant practitioner. Approvals valid for 12 months where the initiation of paliperidone depot injection has been associated with fewer days of intensive intervention than was the case during a corresponding period of time prior to the initiation of an atypical antipsychotic depot injection.

5.2. In making this recommendation, the Advisory Committee considered that while the evidence evaluated was of weak to moderate quality and strength, the improvements in quality of life, improvements in regard to carer burden and positive impact on reducing inequities informed the high recommendation.

Discussion

5.1. The Committee noted that previously this funding application for paliperidone three-monthly was assessed by this Committee and recommended to be funded only if cost neutral to the combined pharmaceutical budget (a positive recommendation). The Committee also noted that it was then further assessed by PTAC where it was recommended to be listed with a low priority, only if cost neutral on a mg-to-mg basis with paliperidone once-monthly and if longer-term financial risks could be addressed. The Committee noted that at the time of these recommendations, it was noted that the three-monthly presentation was non-inferior to the currently funded once-monthly formulation and there were concerns regarding additional cost due to a shift to paliperidone from other anti-psychotic long acting injectables ("depots").

5.2. The Committee noted that schizophrenia is debilitating and associated with medical and psychiatric comorbidities, as well as early mortality. The Committee noted that Māori are approximately three times more likely than non-Māori to experience schizophrenia (Kake et al. Aus NZ J. Psych. 2008;42:941-9). The Committee noted that adherence to anti-psychotic medicines is often an issue.

5.3. The Committee noted that a resubmission was recently received which contained a range of additional data, including 'real-world' evidence to support the use of paliperidone three-monthly. Including information regarding:

5.3.1. Relapse and adherence: Turkoz et al, Li et al, and El Khoury et al which all reported improved adherence in those taking paliperidone three-monthly compared with the once-monthly formulation (Turkoz et al. Poster presented at the Psych Congress. 2021. San Antonio, Texas; Li et al, Ptn Pref Adher. 2021;15:2239-48; El Khoury et al. Neuropsychiatri Dis Treat. 2021;17:3159-70).

5.3.2. Carer burden: Lencer et al reported a statistically significant reduction in carer burden for those caring for people with stable schizophrenia when they transitioned from 1-monthly to 3-monthly paliperidone palmitate (Lencer et al. Compr Psychiatry. 2021;107: doi: 10.1016/j.comppsych.2021.152233.).

5.3.3. Quality of life: Rise et al. which reported qualitative data that paliperidone three-monthly had advantages including less frequent antipsychotic injections, less administration, and less focus on the illness (Rise et al. Nord J Psychiatry. 2021;75:257-65). Pugnor et al. reported reasons that people switched from once-monthly to three-monthly paliperidone included increased patient activity and social involvement, improved frequency and quality of physician- patient and nurse-patient communication, and decreased perceived stigma (Pugnor et al. BMC Psychiatry. 2021;21: doi: 10.1186/s12888-021-03305-z).

5.3.4. Hospitalisations: Garcia-Portilla et al, DerSarkissian et al., Lin et al. which reported better less frequent hospitalisations in those treated with paliperidone three-monthly (Garcia-Portilla et al. Ther Adv Psychopharmacol. 2020;10: doi: 10.1177/2045125320926347; DerSarkissian et al. Clin Ther. 2018;40:1496-508; Lin et al. Curr Med Res Opin. 2021;37:675-83). The Committee noted that the supplier estimated a health sector saving could be achieved if paliperidone three-monthly were funded, primarily due to a reduction in hospitalisations. The Committee considered that any reduction in hospitalisations would be a meaningful benefit with current resource constraints (eg. hospital staffing, specialist availability); however, Members cautioned modelling any potential cost savings from reduced hospitalisations due to the relatively low quality of this evidence and the uncertainty of applicability to New Zealand.

5.4. The Committee considered that overall, the evidence provided in the resubmission was of weak to moderate quality and strength. Members considered that the qualitative data were important and that it aligned with positive clinician views regarding paliperidone three-monthly. Members noted that the vast majority of the evidence included in the resubmission was authored by individuals with substantial conflicts of interest. Members did not discuss the possible impacts of these conflicts on the evidence provided.

5.5. Members considered that the benefits which could occur from the funding of paliperidone three-monthly (eg. reduction in relapses, improved adherence) would be experienced by those most disadvantaged and that as such this proposal may have a positive influence on improving inequities currently observed with schizophrenia. Members also noted that the benefits to carers highlighted by Lencer et al. would meet the wider health need of the whānau and support Māori health outcomes.

5.6. The Committee noted the resubmission included Australian data, which showed the market share of antipsychotic depots before and after the funding of

paliperidone three-monthly. The Committee noted that in Australia, no large shifts in paliperidone use were observed. The Committee noted that aripiprazole depot is funded and holds a large market share in Australia, but it is not currently funded in New Zealand. Members considered that as aripiprazole depot is not currently funded in New Zealand, the presented market share data have low relevance to what may occur in New Zealand if paliperidone three-monthly were funded. The Committee considered, in the absence of aripiprazole depot funding, that if paliperidone three-monthly were funded, it was likely that a shift to paliperidone from other antipsychotic depots and oral antipsychotics would occur.

5.7. The Advisory Committee considered that the below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for paliperidone three-monthly if it were to be funded in New Zealand for schizophrenia. 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	Adults with schizophrenia who have been adequately treated with paliperidone one-monthly depot injection for at least four months.
Intervention	Paliperidone three-monthly depot
Comparator(s)	Paliperidone once-monthly depot
Outcome(s)	Non-inferiority to paliperidone once-monthly Limited potential reduction in hospitalisations
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.	

6. Aripiprazole depot

Discussion

6.1. The Committee noted that the supplier of aripiprazole depot provided a letter in response to the Mental Health Advisory Committee's consideration of aripiprazole depot in September 2021, where it was recommended for funding with a medium priority. The Committee noted that concerns were raised by the supplier regarding the advice on the relative efficacy of aripiprazole depot and references to possible side effects (namely akathisia).

6.2. The Committee noted the additional evidence provided by the supplier relating to efficacy of aripiprazole, as well as additional publications:

6.2.1. Huhn et al. a systematic review and network meta-analysis which compared the efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia (Huhn et al. Lancet 2019; 394:939–51). The Committee noted that this review adequately controlled for placebo effects over time.

6.2.2. Kim et al. a systematic review and meta-analysis, which reported the efficacy and tolerability of oral aripiprazole versus D2 antagonists in the early course of schizophrenia (Kim et al. Schizophrenia. 2021;7, doi.org/10.1038/s41537-021-00158-z).

6.3. Regarding possible side effects, the Committee noted that the risk of akathisia from aripiprazole is well documented in the literature when compared with placebo.

6.4. The Committee considered that the advice it provided in September 2021 regarding aripiprazole depot remained appropriate and did not consider that further consideration or an updated recommendation was required at this point in time, based on the correspondence received from the supplier.

7. Brand changes – mental health medicines

Discussion

7.1. The Committee noted that Pharmac had recently updated its approach to contracting, with a shift from sole supply to principal supply. The Committee noted that this change means that the principal supplier's brand would be the main brand funded in the community and/or bought by DHB hospitals, with an allowance for other brands to be funded by Pharmac.

7.2. The Committee noted that Pharmac was seeking advice regarding brand change communication and the implementation of alternative brand allowances in the context of mental health medicines.

7.3. Members considered that it was important when communicating a brand change that the main stakeholders are identified, mainly prescribers and patients and appropriate communication channels are in place – for example, this could include education forums, collaborations with medical colleges etc. Members also considered that an appropriate balance and consistent messaging between primary and secondary care was important.

7.4. Members considered that appropriate balance was required when communicating a brand change for a mental health medicine. Ie. appropriately informing prescribers and patients, but also not causing undue anxiety where a brand change, in most cases, is not expected objectively on biological grounds to have a therapeutic impact. Members considered that particular care should be taken when communicating regarding changes in medicines used for internalising disorders to not cause undue anxiety.

7.5. The Committee considered, for the medicines highlighted by Pharmac staff, a 5% alternative brand allowance seemed appropriate, and did not anticipate that an incumbent brand would be required to remain listed on the Schedule in the event of a brand change.