Paliperidone

Section: 24. Medicines for mental and behavioural disorders > 24.1. Medicines for psychotic disorders

Codes ATC: N05AX13

Indication	Schizophrenia or other primary psychotic disorders Code ICD11: 6A2Z
INN	Paliperidone
Type de médicament	Chemical agent
Type de liste	Liste de base
Formulations	**Parenteral > General injections > IM:** 25 mg in pre-filled syringe (as palmitate) ; 50 mg in pre-filled syringe (as palmitate) ; 75 mg in pre-filled syringe (as palmitate) ; 100 mg in pre-filled syringe (as palmitate) ; 150 mg in pre-filled syringe (as palmitate)
Historique des statuts LME	Ajouté pour la première fois en 2021 (TRS 1035) Modifié en 2023 (TRS 1049) Modifié en 2025 (TRS 1064)
Sexe	Tous
Âge	Adolescents et adultes
Équivalence thérapeutique	risperidone (Codes ATC: N05AX08) Parenteral > General injections > IM: aripiprazole (Codes ATC: N05AX12) Parenteral > General injections > IM: 300 mg powder and solvent for suspension; 400 mg powder and solvent for suspension
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite sur les brevets.
Wikipédia	Paliperidone
DrugBank	Paliperidone

Recommandation du comité d'experts

The Expert Committee acknowledged that schizophrenia was a complex debilitating psychiatric disorder. It has one of the highest mortality risks of all mental health disorders and affects several aspects of life. The Committee noted that paliperidone once-monthly long-acting injection was currently included on the EML for maintenance treatment of schizophrenia. Listing is with a square box specifying risperidone long-acting injection as a therapeutic alternative. The Committee also noted that use of long-acting injectable antipsychotics required patients to be first stabilized on oral treatment before switching to the injectable preparation. Oral second-generation antipsychotics currently included on the EML for treatment of schizophrenia are risperidone as the class representative, with aripiprazole, olanzapine, paliperidone and quetiapine as therapeutic alternatives. The Committee recognised the potential for continuity between oral aripiprazole and long-acting injectable aripiprazole. The Committee noted from the most recent network meta-analysis presented in the application that long-acting injectable antipsychotics were more effective than placebo in preventing relapse. In head-to-head comparisons, the study found no significant differences between aripiprazole long-acting injection and other long-acting injectable antipsychotics medicines. However, direct heat-to-head trials comparing aripiprazole with other long-acting injectable antipsychotics were lacking. Compared with oral antipsychotics, the Committee noted that data suggest long-acting injectable antipsychotics may offer benefit in terms of reduced risk of hospitalization or

relapse, and better treatment adherence. As regards harms, the Committee noted that the most commonly reported adverse effects of long-acting injectable antipsychotics were extrapyramidal symptoms. Compared with paliperidone or risperidone, aripiprazole has a lower risk of metabolic side-effects and weight gain. The Committee recognized the substantially higher costs of long-acting antipsychotics compared with oral therapies but considered that the higher costs may be offset in part by reduced total cost of care for schizophrenia and fewer hospitalizations. There was limited information about the comparative costs of aripiprazole, paliperidone and risperidone long-acting injections. However, the Committee assumed that aripiprazole was likely to be more expensive than the others, since generics are available for paliperidone and risperidone, but not yet for aripiprazole. The Committee agreed with the comments made by Médecins Sans Frontières, that aripiprazole long-acting injection may be a preferred therapeutic alternative to paliperidone than risperidone long-acting injection in low- and middle-income countries and in humanitarian contexts. Unlike risperidone, which requires reconstitution, cold chain and refrigerated storage, and administration every 2 weeks, aripiprazole long-acting injection is available in a prefilled syringe formulation which does not require reconstitution, can be stored at room temperature and is administered once per month. Based on these considerations, the Expert Committee recommended the inclusion of aripiprazole once-monthly long-acting injection on the core list of the EML for the maintenance treatment of adults with schizophrenia based on acceptable evidence of similar efficacy and a potentially lower risk of metabolic adverse effects compared with other long-acting injectable antipsychotics currently included on the EML. Listing is recommended for aripiprazole as a therapeutic alternative under the square box listing for paliperidone once-monthly long-acting injection.

Contexte

Aripiprazole long-acting injection has not previously been evaluated for inclusion in the EML. In 2021, the Expert Committee recommended the addition of paliperidone once-monthly long-acting injection to the core list of the EML for maintenance treatment of schizophrenia in adults stabilized on oral therapy. A square box listing was recommended specifying risperidone long-acting injection as a therapeutic alternative. The Committee considered that long-acting injectable antipsychotic medicines were a valuable treatment option to increase adherence to treatment and reduce relapse in adults with schizophrenia and related psychotic disorders. The Committee also noted with concern the uncertainty of current and future availability of fluphenazine injection, which was the only long-acting injectable antipsychotic medicine included on the EML at that time and considered that the availability of alternative medicines would be important to meet the public health need for such treatments. The Committee noted that long-acting injectable antipsychotic medicines are an established treatment option for schizophrenia and are recommended in existing WHO Mental Health Gap Action Programme (mhGAP) guidelines. In particular, the Committee acknowledged that long-acting injectable antipsychotic medicines are useful in low-resource settings, where many factors might impede regular monitoring and follow-up of patients. The Committee noted that the available data suggested benefits of long-acting injectable antipsychotic medicines versus oral antipsychotic medicines in preventing hospitalization or relapse, especially in populations with low treatment adherence. The effectiveness and overall safety of first-generation and second-generation antipsychotic medicines were similar. The availability of agents with different side-effect profiles may support the selection of one treatment over another given a patient’s clinical status and vulnerabilities (1). In 2023, the Expert Committee considered an application for the inclusion of paliperidone 3 monthly long-acting injection on the EML for maintenance treatment of schizophrenia. The 2023 Committee recognized that long-acting injectable antipsychotic medicines were an important treatment option for some patients with schizophrenia. It recalled the recommendation made by the 2021 Expert Committee to include paliperidone once-monthly long-acting injection on the EML for this indication, with risperidone long-acting injection as a therapeutic alternative among second-generation antipsychotics. The Committee also noted the separate application to the 2023 meeting proposing therapeutic alternatives to long-acting injections of first-generation antipsychotics. The Committee noted that compared with the 1 month formulation, the 3-month formulation had evidence of similar clinical efficacy and safety and may offer advantages to patients in terms of fewer injections. However, the Committee noted that the 3-month formulation was recommended for use only in patients who had been adequately treated with the once-monthly formulation and demonstrated benefit from and tolerance to it for at least 4 months. The Committee was

therefore concerned that both strength formulations would need to be available for appropriate treatment and considered that the more limited availability of the 3-month formulation in low- and middle-income countries would be problematic. In addition, the Committee noted that the 3 month formulation was more highly priced and was not yet available in generic forms, nor included in current WHO mhGAP guidelines. Based on these considerations, the Expert Committee did not recommend the inclusion of paliperidone 3-month long-acting injection on the EML for maintenance treatment of schizophrenia (2). Oral aripiprazole was included in the EML in 2023 as one of four therapeutic alternatives to oral risperidone for the treatment of schizophrenia, in alignment with recommendations in the 2023 WHO mhGAP guideline (2).

Pertinence pour la santé publique

Schizophrenia is a chronic, complex, progressive and heterogeneous psychiatric disorder that typically manifests behaviourally in late adolescence or early adulthood (3, 4). It leads to psychosis and significant disability, affecting personal, family, social, educational and occupational functioning (5). People diagnosed with schizophrenia often face stigma, discrimination and human rights violations (5, 6). According to the Global Burden of Disease study, the incidence of new schizophrenia cases rose by 37% from 1990 to 2019, reaching 1.3 million individuals. The age-standardized global incidence of schizophrenia was 16.31 per 100 000 individuals in 2019 and showed considerable geographic variation. The age-standardized global prevalence of schizophrenia in 2019 was reported to be 287.4 per 100 000 individuals (7). Schizophrenia was associated with the highest percentage increase in the prevalence rate compared with other mental disorders between 1990 and 2019 in low- and middle-income countries. A study conducted to determine the burden of mental disorders in Middle Eastern and North African countries determined that the prevalence of schizophrenia increased by 33.5% between 1990 to 2019 (8). Schizophrenia was ranked the 20th leading cause of years lived with disability (YLDs) within mental health disorders in 2019. Schizophrenia accounted for the third largest proportion of disability-adjusted life years (DALYs) due to mental health disorders in 2019, at 12.2% (7). The rate of DALYs due to mental disorders in low- and middle-income countries are increasing, with a 13.9% increase seen over 30 years. Among all mental disorders, schizophrenia had the third highest increase, with a 33.0% rise in DALY rates (8). Schizophrenia has one of the highest mortality risks among psychiatric disorders, with a 2.9 fold increase in all-cause mortality, and individuals with schizophrenia die 15–20 years earlier than the general population (9). A 2017 systematic review and meta-analysis investigating years of potential life lost and life expectancy in schizophrenia reported that the overall weighted global average life expectancy for persons with schizophrenia was 64.7 years and was lower for men than women (59.9 years versus 67.6 years). The review also reported that life expectancy was the lowest in Asia and Africa, indicating disparities in health outcomes and access to health-care services compared with other regions (10).

Bénéfices

Systematic reviews A 2021 systematic review and meta-analysis of 137 studies (32 randomized controlled trials, 8577 participants; 65 cohort studies, 377 447 participants; and 40 pre–post studies, 11 295 participants) evaluated the comparative benefits of long-acting injectable versus oral antipsychotics for the treatment of schizophrenia (11). Data specific to aripiprazole were not reported separately. The primary outcome assessed was risk of hospitalization or relapse, which was found to be significantly lower for long-acting injectable antipsychotics compared with oral antipsychotics in each study design group: risk ratio (RR) 0.88, 95% confidence interval (CI) 0.79 to 0.99 (29 randomized controlled trials, 7833 participants); RR 0.92, 95% CI 0.88 to 0.98 (44 cohort studies, 106 136 participants); and RR 0.44, 95% CI 0.39 to 0.51 (28 pre–post studies, 17 876 participants). A 2022 systematic review and network meta-analysis of 92 randomized controlled trials (22 645 participants) compared long-acting injectable with oral antipsychotics for relapse prevention in schizophrenia-spectrum disorders (12). For the primary efficacy outcome of relapse prevention, there was high confidence that aripiprazole (relative risk (RR) 0.35, 95% CI 0.22 to 0.49) and olanzapine (RR 0.35, 95% CI 0.23 to 0.54) long-acting injections were significantly more effective than placebo. There was also moderate confidence that paliperidone 3-monthly and once-monthly long-acting injections were significantly more effective than placebo: RR 0.24 (95% CI 0.13 to 0.42) and RR 0.36 (95% CI 0.24 to 0.53), respectively. There was low confidence that risperidone long-acting injection was

significantly more effective than placebo for relapse prevention (RR 0.35, 95% CI 0.25 to 0.50). In head-to-head comparisons, no significant differences were seen between aripiprazole long-acting injection and other antipsychotics. For the outcome of tolerability (i.e. the proportion of participants who discontinued the trial due to adverse events), only oral olanzapine was associated with a significant benefit compared with placebo (RR 0.61, 95% CI 0.41 to 0.90; low confidence in the evidence). A 2021 systematic review and network meta-analysis of 78 randomized controlled trials (11 505 participants) compared different long-acting injectable antipsychotics for relapse prevention and acceptability in maintenance treatment of adults with non-affective psychoses (13). Primary outcomes were the proportion of patients who experienced at least one relapse and the proportion of patients who dropped out of trials for any reason (acceptability). The primary analysis found that most long-acting injectable antipsychotics evaluated were significantly more effective than placebo for relapse prevention, including aripiprazole (RR 0.29, 95% CI 0.21 to 0.39; moderate-certainty evidence), and others currently included on the EML. Paliperidone 3-monthly, aripiprazole and flupenthixol ranked best according to the mean surface under the cumulative ranking curve (SUCRA), with scores of 80.2%, 78.0% and 65.4%, respectively. In head-to-head comparisons, aripiprazole was significantly more effective at preventing relapse than haloperidol (RR 0.51, 95% CI 0.28 to 0.93). However, significant differences between aripiprazole and other second-generation antipsychotics were not reported: RR 0.74 (95% CI 0.51 to 1.08) versus paliperidone once-monthly and RR 0.83 (95% CI 0.54 to 1.27) versus risperidone. For the outcome of acceptability, most long-acting injectable antipsychotics evaluated were significantly more effective than placebo including aripiprazole (RR 0.49, 95% CI 0.41 to 0.58; moderate-certainty evidence) and others currently included on the EML. Zuclopenthixol, aripiprazole and perphenazine ranked best according to SUCRA with scores of 89.6%, 86.1% and 79.2%, respectively. In head-to-head comparisons, aripiprazole was significantly more acceptable than bromperidol, fluphenazine, paliperidone 3-monthly, pipothiazine and risperidone. Randomized trials The application also presented brief overviews of the findings of individual company-funded randomized trials that compared aripiprazole once-monthly with placebo and other antipsychotics (14–20). Real-world studies An online survey of 500 psychiatrists in Australia, Canada, France, Italy, Spain and the United Kingdom gathered real-world evidence of functional improvements with long-acting injectable antipsychotic treatment in recent-onset schizophrenia (21). Data were collected for 1000 patients receiving aripiprazole once monthly 400 mg and 1000 patients receiving paliperidone once monthly. Global assessment of functioning scores increased from baseline by 19.7 points and 16.3 points in patients treated with aripiprazole and paliperidone, respectively. Personal and social performance ratings of treatment (deficits in self-care and disturbing and aggressive behaviours) were generally mild or borderline moderate for both groups. A 2020 pharmaceutical-company-funded, retrospective, observational cohort study in Japan evaluated treatment persistence with aripiprazole once monthly versus oral aripiprazole (22). Patients receiving aripiprazole once monthly injection were significantly less likely to discontinue treatment than those in the total oral aripiprazole group (adjusted hazard ratio (HR) 0.54, 95% CI 0.53 to 0.86), and those with at least two prescription records of oral aripiprazole (adjusted HR 0.67, 95% CI 0.53 to 0.86). Other subgroup analyses had similar findings.

Torts

A 52-week, company-funded, open-label study assessed the long-term safety and tolerability of aripiprazole once monthly injection 400 mg for the maintenance of schizophrenia (17). Patients were either previously enrolled in one of two randomized controlled trials of aripiprazole once monthly (n = 984) or new patients (n = 194). The study included an oral conversion phase, an oral stabilization phase and an open-label maintenance phase. During the maintenance phase, 934/1081 (86.4%) patients received aripiprazole 400mg for ≥ 6 months and 826/1081 (76.4%) patients received treatment for ≥ 12 months. Most patients (990/1081, 91.6%) started treatment at the 400 mg dose and maintained this dose. About two thirds of patients experienced treatment-emergent adverse effects; most were mild or moderate in severity. The most commonly reported treatment-emergent adverse effects were any extrapyramidal symptoms (9.0%), headache (7.6%) and nasopharyngitis (7.0%). Serious and severe treatment-emergent adverse effects were reported in 8.8% and 7.3% of patients, respectively. Treatment-emergent adverse effects led to study discontinuation in 6.3% of patients. Treatment-emergent adverse effects that occurred in ≥ 1% of patients and were classified as serious, severe or leading to study discontinuation included psychotic disorder and schizophrenia (serious: 1.4% and 1.9%, respectively; severe: 1.2% and 1.3%,

respectively; leading to study discontinuation: 1.3% and 1.7%, respectively). No clinically relevant mean changes from baseline were seen in serum chemistry, haematology, urinalysis, insulin, fasting insulin, vital signs (including blood pressure, heart rate, body temperature, waist circumference and body mass index) or electrocardiogram parameters during the aripiprazole once monthly maintenance phase. A moderately higher incidence of potentially clinically relevant weight gain or loss (≥ 7% change from baseline) was seen at the last visit in new patients compared with patients who were enrolled from the randomized controlled trials. At the last visit of the maintenance phase, potentially clinically relevant prolactin concentrations (above the upper limit of normal) were reported in 2.1% of all patients. Extrapyramidal symptom rating scale scores remained stable throughout the maintenance phase. In the 2022 network meta-analysis comparing the effectiveness and tolerability of oral and long-acting injectable antipsychotics, common antipsychotic-related adverse events were assessed as a secondary tolerability outcome (12). Compared with placebo: risperidone long-acting injection, oral paliperidone, oral lurasidone and oral risperidone were associated with a significantly higher risk of sedation; oral aripiprazole, olanzapine long-acting injection, oral olanzapine and paliperidone long-acting injection (1-monthly and 3-monthly) were associated with a significantly higher risk of weight gain; oral haloperidol, fluphenazine long-acting injection and pipothiazine long-acting injection were associated with a significantly higher risk of extrapyramidal symptoms; oral haloperidol, haloperidol long-acting injection and oral trifluoperazine were associated with a significantly higher risk of akathisia; oral olanzapine, olanzapine long-acting injection, paliperidone long-acting injection (1-monthly and 3-monthly), risperidone long-acting injection, oral risperidone and oral paliperidone-overall survival were associated with a significantly higher risk of hyperprolactinaemia; and oral olanzapine, olanzapine long-acting injection, oral asenapine, paliperidone long-acting injection (3-monthly) and oral risperidone were associated with a significantly lower risk of insomnia. No antipsychotics showed a higher risk of QTc prolongation and tardive dyskinesia as compared to placebo, although CIs were imprecise for most comparisons.

Rapport coût/efficacité

Data from the United States in 2019 indicate that schizophrenia was associated with an economic burden of 343.2 billion United States dollars (24). Schizophrenia also poses a high economic burden in low- and middle-income countries. Indirect costs are reported to account for 50–90% of the economic burden of schizophrenia (25). The direct costs of schizophrenia include inpatient/outpatient care, drug costs, treating and managing side-effects and comorbidities, rehabilitation, and social welfare administration. The indirect costs of schizophrenia include unemployment, reduced productivity at work, premature mortality, inability to live independently and financial impacts on family life (25–27). The economic impact of aripiprazole once-monthly was evaluated in various studies that evaluated the effect on hospitalization rate versus oral antipsychotic therapy (28, 29), comparative 6-month costs and outcomes versus paliperidone once-monthly (30) and cost–effectiveness versus paliperidone once-monthly in the treatment of schizophrenia (31). These studies were all conducted in the United States. They found significant reductions in total psychiatric hospitalization rates and cost-of-care savings for health plans (as a result of reduced psychiatric hospitalizations) with aripiprazole once-monthly, and economic dominance of aripiprazole once-monthly over paliperidone once monthly. A 2023 analysis modelled the cost–effectiveness of aripiprazole once monthly versus paliperidone once-monthly in the treatment of stable schizophrenia from a societal perspective in Thailand over a lifetime horizon (32). The resultant incremental cost–effectiveness ratios were similar for each treatment: 81 652.85 Thai baht/QALY gained and 81 330.94 Thai baht/QALY gained for aripiprazole and paliperidone, respectively. The authors noted that if the cost of aripiprazole once-monthly decreased by 2%, it would become the dominant strategy. The application reported list prices for aripiprazole once-monthly 400 mg prefilled syringe or vial ranging from 106 euros (€) in Indonesia to €420 in Germany. The application stated that following patent expiration in October 2024, generic alternatives may enter the market and lead to price reductions. Comparative costs of other long-acting injectable antipsychotic medicines were not reported.

Directives de l'OMS

The 2023 WHO mhGAP guideline for mental, neurological and substance use disorders includes a conditional recommendation that long-acting injection antipsychotic medicines (fluphenazine, haloperidol, paliperidone,

risperidone and zuclopenthixol) should be considered as an alternative to oral antipsychotic medicines for adults with psychotic disorders (including schizophrenia) requiring long-term treatment, carefully balancing effectiveness, side-effects and individual preference (moderate-certainty evidence) (23). The WHO guideline also includes a strong recommendation that adults with a psychotic disorder (including schizophrenia) be offered oral antipsychotic medicines (namely aripiprazole, chlorpromazine, haloperidol, olanzapine, paliperidone, quetiapine and risperidone), carefully balancing effectiveness, side-effects and individual patient preferences (moderate-certainty evidence). Various national and professional society guidelines recommend offering long-acting injectable antipsychotic medicines to individuals with schizophrenia who need long-term treatment, request such treatments or who have difficulties adhering to medication.

Disponibilité

The application reported that aripiprazole once-monthly injection (300 mg and 400 mg) has regulatory approval in 62 (primarily high-income) countries/territories globally, with market availability in 58 of them. Patent expiry is reported in October 2024. Generic formulations are not currently available.

Autres considérations

The Department of Mental Health, Brain Health and Substance Use reviewed and provided comments on the application. The technical department highlighted that aripiprazole long-acting injection was similar to other long-acting injection antipsychotics currently included on the EML (risperidone and paliperidone) for clinical efficacy and acceptability. However, aripiprazole long-acting injection may have advantages over the others in terms of tolerability (less weight gain), handling and storage. The technical department also advised that current costs were high and availability in low- and middle-income countries was limited. Aripiprazole long-acting injection is not currently included in the WHO mhGAP guidelines and the technical department did not think that there was a compelling case for the inclusion of aripiprazole long-acting injection on the EML at this time.

1. The selection and use of essential medicines. Report of the WHO Expert Committee, 2021 (including the 22nd WHO Model List of Essential Medicines and the 6th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization; 2021 (WHO Technical Report Series, No. 1035; https://apps.who.int/iris/handle/10665/351172). Licence: CC BY-NC-SA 3.0 IGO.
2. The selection and use of essential medicines. Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2023 (including the 23rd WHO Model List of Essential Medicines and the 9th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization; 2024 (WHO Technical Report Series, No. 1049; https://iris.who.int/handle/10665/376570). Licence: CC BY-NC-SA 3.0 IGO.
3. He H, Liu Q, Li N, Guo L, Gao F, Bai L et al. Trends in the incidence and DALYs of schizophrenia at the global, regional and national levels: results from the Global Burden of Disease Study 2017. Epidemiol Psychiatr Sci. 2020;29:e91 (https://doi.org/10.1017/s2045796019000891).
4. Luvsannyam E, Jain MS, Pormento MKL, Siddiqui H, Balagtas ARA, Emuze BO et al. Neurobiology of schizophrenia: a comprehensive review. Cureus. 2022;14(4):e23959 (https://doi.org/10.7759/cureus.23959).
5. Schizophrenia [internet]. Geneva: World Health Organization; 2022 (Fact sheet; https://www.who.int/news-room/fact-sheets/detail/schizophrenia).
6. Hoftman GD. The burden of mental illness beyond clinical symptoms: impact of stigma on the onset and course of schizophrenia spectrum disorders. Am J Psychiatry Resid J. 2016;11(4):5–7 (https://doi.org/10.1176/appi.ajp-rj.2016.110404).
7. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry. 2022;9(2):137–50 (https://doi.org/10.1016/s2215-0366(21)00395-3).
8. Effatpanah M, Nakhostin-Ansari A, Gorgani F, Khotbehsara ST, Seifi S, Nasoori H et al. Burden and epidemiology of mental disorders in the Middle East and North Africa from 1990 to 2019: findings from the Global Burden of Disease Study. Balkan Med J. 2024;41(2):121–9 (https://doi.org/10.4274/balkanmedj.galenos.2024.2023-11-55).
9. Correll C, Solmi M, Croatto G, Schneider L, Rohani-Montez S, Fairley L et al. Mortality in people with schizophrenia: a systematic review and meta-analysis of relative risk and aggravating or attenuating factors. World Psychiatry. 2022;21(2):248–71 (https://doi.org/10.1002/wps.20994).
10. Hjorthøj C, Stürup AE, McGrath JJ, Nordentoft M. Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. Lancet Psychiatry. 2017;4(4):295–301 (https://doi.org/10.1016/s2215-0366(17)30078-0).
11. Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre-post studies. Lancet Psychiatry. 2021;8(5):387–404 (https://doi.org/10.1016/s2215-0366(21)00039-0).
12. Ostuzzi G, Bertolini F, Tedeschi F, Vita G, Brambilla P, Del Fabro L et al. Oral and long-acting antipsychotics for relapse prevention in schizophrenia-spectrum disorders: a network meta-analysis of 92 randomized trials including 22,645 participants. World Psychiatry. 2022;21(2):295–307 (https://doi.org/10.1002/wps.20972).

13. Ostuzzi G, Bertolini F, Del Giovane C, Tedeschi F, Bovo C, Gastaldon C et al. Maintenance treatment with long-acting injectable antipsychotics for people with nonaffective psychoses: a network meta-analysis. Am J Psychiatry. 2021;178(5):424–36 (https://doi.org/10.1176/appi.ajp.2020.20071120).
14. Kane JM, Sanchez R, Perry PP, Jin N, Johnson BR, Forbes RA et al. Aripiprazole intramuscular depot as maintenance treatment in patients with schizophrenia: a 52-week, multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2012;73(5):617–24 (https://doi.org/10.4088/JCP.11m07530).
15. Fleischhacker WW, Sanchez R, Perry PP, Jin N, Peters-Strickland T, Johnson BR et al. Aripiprazole once-monthly for treatment of schizophrenia: double-blind, randomised, non-inferiority study. Br J Psychiatry. 2014;205(2):135–44 (https://doi.org/10.1192/bjp.bp.113.134213).
16. Naber D, Hansen K, Forray C, Baker RA, Sapin C, Beillat M et al. Qualify: a randomized head-to-head study of aripiprazole once-monthly and paliperidone palmitate in the treatment of schizophrenia. Schizophr Res. 2015;168(1–2):498–504 (https://doi.org/10.1016/j.schres.2015.07.007).
17. Peters-Strickland T, Baker RA, McQuade RD, Jin N, Eramo A, Perry P et al. Aripiprazole once-monthly 400 mg for long-term maintenance treatment of schizophrenia: a 52-week open-label study. NPJ Schizophr. 2015;1:15039 (https://doi.org/10.1038/npjschz.2015.39).
18. Kane JM, Schooler NR, Marcy P, Correll CU, Achtyes ED, Gibbons RD et al. Effect of long-acting injectable antipsychotics vs usual care on time to first hospitalization in early-phase schizophrenia: a randomized clinical trial. JAMA Psychiatry. 2020;77(12):1217–24 (https://doi.org/10.1001/jamapsychiatry.2020.2076).
19. Kane JM, Peters-Strickland T, Baker RA, Hertel P, Eramo A, Jin N et al. Aripiprazole once-monthly in the acute treatment of schizophrenia: findings from a 12-week, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2014;75(11):1254–60 (https://doi.org/10.4088/JCP.14m09168).
20. Potkin SG, Raoufinia A, Mallikaarjun S, Bricmont P, Peters-Strickland T, Kasper W et al. Safety and tolerability of once monthly aripiprazole treatment initiation in adults with schizophrenia stabilized on selected atypical oral antipsychotics other than aripiprazole. Curr Med Res Opin. 2013;29(10):1241–51 (https://doi.org/10.1185/03007995.2013.821973).
21. Such P, Olivares JM, Arias L, Troels Berg M, Madera J. Online survey of clinical practice in patients with schizophrenia treated with long-acting injectable aripiprazole or paliperidone palmitate. Neuropsychiatr Dis Treat. 2021;17:1881–92 (https://doi.org/10.2147/ndt.S303292).
22. Iwata N, Inagaki A, Sano H, Niidome K, Kojima Y, Yamada S. Treatment persistence between long-acting injectable versus orally administered aripiprazole among patients with schizophrenia in a real-world clinical setting in Japan. Adv Ther. 2020;37(7):3324–36 (https://doi.org/10.1007/s12325-020-01396-w).
23. Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders. Geneva, World Health Organization; 2023 (https://iris.who.int/handle/10665/374250). Licence: CC BY-NC-SA 3.0 IGO.
24. Kadakia A, Catillon M, Fan Q, Williams GR, Marden JR, Anderson A et al. The economic burden of schizophrenia in the United States. J Clin Psychiatry. 2022;83(6):22m14458 (https://doi.org/10.4088/JCP.22m14458).
25. Kotzeva A, Mittal D, Desai S, Judge D, Samanta K. Socioeconomic burden of schizophrenia: a targeted literature review of types of costs and associated drivers across 10 countries. J Med Econ. 2023;26(1):70–83 (https://doi.org/10.1080/13696998.2022.2157596).
26. Pilon D, Patel C, Lafeuille M-H, Zhdanava M, Lin D, Côté-Sergent A et al. Prevalence, incidence and economic burden of schizophrenia among Medicaid beneficiaries. Curr Med Res Opin. 2021;37(10):1811–9 (https://doi.org/10.1080/03007995.2021.1954894).
27. Waters HC, Stellhorn R, Touya M, Fitzgerald H, Bhattacharjee S, Citrome L. The effects of early initiation of aripiprazole once-monthly on healthcare resource utilization and healthcare costs in individuals with schizophrenia: real-world evidence from US claims data. J Med Econ. 2023;26(1):316–25 (https://doi.org/10.1080/13696998.2023.2178770).
28. Kane JM, Zhao C, Johnson BR, Baker RA, Eramo A, McQuade RD et al. Hospitalization rates in patients switched from oral anti-psychotics to aripiprazole once-monthly: final efficacy analysis. J Med Econ. 2015;18(2):145–54 (https://doi.org/10.3111/13696998.2014.979936).
29. Wilson M, Gutierrez B, Offord SJ, Blanchette CM, Eramo A, Earnshaw S et al. Inpatient resource use and costs associated with switching from oral antipsychotics to aripiprazole once-monthly for the treatment of schizophrenia. Drugs Context. 2016;5:212273 (https://doi.org/10.7573/dic.212273).
30. Sapin C, Hartry A, Kamat SA, Beillat M, Baker RA, Eramo A. Pharmacoeconomic comparison of aripiprazole once-monthly and paliperidone palmitate from a head-to-head clinical trial in schizophrenia: a US analysis. Drugs Context. 2016;5:212301 (https://doi.org/10.7573/dic.212301).
31. Citrome L, Kamat SA, Sapin C, Baker RA, Eramo A, Ortendahl J et al. Cost–effectiveness of aripiprazole once-monthly compared with paliperidone palmitate once-monthly injectable for the treatment of schizophrenia in the United States. J Med Econ. 2014;17(8):567–76 (https://doi.org/10.3111/13696998.2014.917089).
32. Ueapanjasin P, Thavornwattanayong W, Lertsirimunkong J, Chaiyakittisopon K. Cost–effectiveness analysis of long-acting injectable once-monthly of aripiprazole compared with long-acting injectable once-monthly paliperidone palmitate for the treatment of stable schizophrenia patients in Thailand. Siriraj Med J. 2023;75(10):725–35 (https://doi.org/10.33192/smj.v75i10.264770).

