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SCHIZOPHRENIC PATIENTS ON LONG-TERM ORAL/ TOPICAL ANTIPSYCHOTIC TREATMENT WITHOUT A TRIAL OF ATYPICAL LONG-ACTING INJECTABLE THERAPY: A TENNCARE INITIATIVE

Schizophrenia is one of the top 20 causes of disability worldwide with a lifetime prevalence of approximately 0.7%. Patients with schizophrenia are at risk for increased mortality and shortened life span.[1] Typical and atypical antipsychotic agents are FDA-approved for the treatment of schizophrenia and available in multiple dosage forms (oral, topical, injectable). Long-acting injectable (LAI) atypical antipsychotics are associated with decreased hospitalizations, fewer relapses requiring hospitalization, a decrease in ER visits, and increased compliance when compared to oral antipsychotic therapy.[2,3] The American Psychiatric Association Practice Guidelines for the Treatment of Patients With Schizophrenia recommend that patients receive treatment with a LAI antipsychotic if they prefer such treatment or if they have a history of poor or uncertain adherence.[1] In a recent study of newly diagnosed schizophrenic patients, LAIs were found to have a 47% reduction in the risk of suicide mortality, as well as a decrease in the number of suicide attempts in those patients that switched to LAIs in the first two years of treatment versus those that maintained oral therapy.[4] Due to these recommendations and improved clinical outcomes, TennCare in collaboration with Optum Rx, TennCare's Pharmacy Benefit Manager (PBM), have developed a multimodal program focused on encouraging LAI antipsychotic utilization and improving schizophrenic patient outcomes.

Schizophrenia is a serious mental illness typically diagnosed between 16 and 30 years of age. Schizophrenia is often associated with three main categories of symptoms: positive (psychotic), negative, and cognitive. Positive symptoms include hallucinations, delusions, thought disorders, and movement disorders. Negative symptoms are associated with loss of motivation, loss of interest, withdrawal, difficulty in showing emotions, and loss of normal regular functioning. Cognitive symptoms are demonstrated by a lack of attention, concentration, and memory.[5] Due to its severe and persistent symptoms, schizophrenia is associated with significant health, social, and economic burdens with estimated costs more than $150 billion annually in the United States (based on 2013 data).[1]

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LAI antipsychotics are a treatment option for schizophrenia administered either intramuscularly or subcutaneously every two weeks to every six months depending on the agent and formulation. While typical (first-generation) antipsychotic LAI formulations are available, this newsletter will focus on only the second-generation, atypical antipsychotic LAI formulations as they were developed to reduce extrapyramidal side effects more commonly seen in the typical antipsychotics and increase efficacy (but patients on typicals and atypicals will be considered for future interventions). LAI antipsychotics exert their effects by exhibiting central dopamine and serotonin receptor antagonism, which is beneficial for both positive and negative symptoms of schizophrenia. Currently, no head-to-head efficacy studies exists between the LAI antipsychotics, and selection of LAI is based on patient-specific factors and side effect profiles. See the table below for the currently available LAI atypical antipsychotics.[6]

A recent study by Huang CY et al., demonstrated that even in early schizophrenic disease, transitioning from oral therapy to LAIs is beneficial in decreasing suicide mortality risk by 47%.[4]

Long-Acting Atypical Injectable Drug Name[7,8,9,10]	Doses Available	Administration	Duration of Injection
Abilify Asimtufii® (aripiprazole)	720mg; 960mg	IM	2 months
Abilify Maintena® (aripiprazole)	300mg; 400mg	IM	1 months
Aristada® (aripiprazole)	441mg/1.6mL; 662mg/2.4mL; 882mg/3.2mL; 1064mg/3.9mL	IM	6 weeks- 2 months
Invega Hafyera® (paliperidone)	1092mg/3.5mL; 1560mg/5mL	IM	6 months
Invega Sustenna® (paliperidone)	39mg/0.25mL/; 78mg/0.5mL; 117mg/0.75mL; 156mg/mL; 234mg/1.5mL	IM	1 month
Invega Trinza® (paliperidone)	273mg/0.88mL; 410mg/1.32mL; 546mg/1.75mL; 819mg/2.63mL	IM	3 months
Perseris (risperidone)	90mg; 120mg	Subcutaneous	1 month
Risperdal Consta® (risperidone)	12.5mg; 25mg; 37.5mg; 50mg	IM	2 weeks
Uzedy® (risperidone)	50mg/0.14mL; 75mg/0.21mL; 100mg/0.28mL; 125mg/0.35mL; 150mg/0.42mL; 200mg/0.56mL; 250mg/0.7mL	Subcutaneous	1-2 months
Zyprexa Relprevv® (olanzapine)	210mg; 300mg; 405mg	IM	4 weeks

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Common side effects for antipsychotic medications as listed by the FDA include:

- Drowsiness/dizziness/restlessness
- Weight gain/metabolic syndrome (more common in atypical agents)
- Dry mouth
- Constipation
- Nausea/vomiting
- Blurred vision
- Hypotension
- Seizures
- Changes in white blood cell counts
- Dystonias/tardive dyskinesia (more common in typical agents)

Antipsychotics are the cornerstone of therapy in patients with schizophrenia, bipolar disorder, and other mood disorders. Treatment with antipsychotics has been shown to decrease hospitalizations and improve morbidity and mortality rates, but serious side effects can be a deterrent to therapy in certain individuals. Some of these side effects can be easily identified and intervened on to prevent any long-term consequences, such as those associated with metabolic syndrome. Guidelines recommend consistent monitoring for metabolic syndrome in patients utilizing antipsychotics. Current recommendations include metabolic monitoring via blood glucose or HbA1c, fasting lipid panel, waist circumference, and blood pressure all of which should be measured at baseline, 12 weeks, and yearly thereafter.[1]

LAI antipsychotics provide many benefits for patients but continue to be underutilized. LAIs provide assurance to prescribers that their patients are compliant with therapy as prescribers are immediately aware of missed doses. Less frequent dosing with healthcare provider administration leads to increased patient adherence. LAIs are associated with the following benefits due to their increased compliance and earlier opportunity for prescriber intervention should a missed dose occur:

- Decreased hospitalizations
- Decreased emergency department visits
- Decreased suicide mortality
- Decreased discontinuation of therapy
- Increased sense of symptom control
- Higher satisfaction with less frequent dosing[1]

A recent study by Huang CY et al., demonstrated that even in early schizophrenic disease, transitioning from oral therapy to LAIs is beneficial in decreasing suicide mortality risk by 47%.[4] The benefits of LAIs have led to the American Psychiatric Association Practice Guidelines for the Treatment of Patients With Schizophrenia recommendations that patients receive treatment with a LAI antipsychotic if they prefer such treatment or if they have a history of poor or uncertain adherence.[1]

The fee-for-service (FFS) pharmacy program performed a claims review of patients 18 years of age and older with a diagnosis of schizophrenia between January 1, 2022, and December 31, 2022. To be included in the analysis, patients must have utilized at least 60 days of oral, topical, or injectable typical or atypical antipsychotic therapy. Patients utilizing clozapine therapy were excluded. During this reporting period, 36,422 unique patients (93%) were identified on oral, topical, or short-acting injectable antipsychotic therapy without a trial of LAI atypical antipsychotic therapy. These patients had a total of 291,188 claims totaling $86,383,286.67. There were 2,572 unique patients (7%) identified as utilizing LAI therapy with 35,744 claims totaling $49,032,894,10 (dollar total includes other antipsychotic therapy utilized with LAI therapy).

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TennCare in collaboration with Optum Rx, have developed a multimodal program focused on deploying a customized set of clinical benefit, and educational interventions designed to move schizophrenic patients from non-compliance with antipsychotic medications (specifically typical and atypical antipsychotics) to compliance. This program focuses on improving patient outcomes by reducing emergency department visits and inpatient hospitalizations, improving adherence, improving coordination of care by increasing partnership with managed care plans, and lowering total cost of care. This program includes a multimodal approach to improving outcomes, with several targeted clinical programs. In an effort to ease access to LAI agents and remove further barriers to use, prior authorization for these agents were updated to capture important safety parameters, and several LAI antipsychotic options were moved to preferred status. A retrospective drug utilization review (retro-DUR) program was initiated to encourage utilization of LAIs in patients with history of oral or topical agents without previous trials of LAIs. Various educational programs have been initiated and will continue to educate prescribers and pharmacists on the benefits of LAIs, including this Newsletter, and future live or CE programs. In the coming months, TennCare Provider Liaison Pharmacists will visit selected prescribers with patients that have either had hospitalizations due to non-compliance or issues with antipsychotic compliance for direct outreach on potential LAI utilization. TennCare and Optum Rx are excited to partner with the prescriber community in the efforts to improve schizophrenic outcomes in our patients and appreciate the continued efforts made by our prescriber community.

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THE TENNCARE PHARMACY PROGRAM RETROSPECTIVE DRUG UTILIZATION REVIEW PROCESS

Retrospective drug utilization review (retro-DUR) interventions are an important aspect of the TennCare Pharmacy Program as they promote the synthesis of information which then leads to identified health outcomes. The TennCare Pharmacy Program currently utilizes retro-DUR interventions in the form of provider contact through letter or fax. After evaluation of TennCare Pharmacy claims data, therapeutic areas of opportunity are identified and presented for review and approval by the TennCare Drug Utilization Review Board. After implementation of the new retro-DUR initiative, submitted prescription claims that meet the established criteria will generate a faxed notification letter to the physician(s) involved. This faxed intervention letter is both educational and informative to providers regarding their patient's medication therapy. After a defined, established period of time, a review is performed to determine the outcomes of the retro-DUR program initiative. The outcomes from these types of reviews provide information for developing future prospective standards and interventions to promote optimal patient care. The Medicaid program can then take action upon these outcomes to foster appropriate, quality care for its members.

Despite appearing more costly when dispensing in the pharmacy, TennCare, as well as other State Medicaid pharmacy programs, receive Federal Rebate dollars after dispensing making these brand agents much more cost effective for the program.

WHY DOES TENNCARE PREFER BRAND DRUGS OVER THEIR GENERIC ALTERNATIVES?

Due to best price and inflationary penalties, many brand name products that participate in the Medicaid Federal Drug Rebate Program find themselves in a position of being significantly cheaper than their generic counterparts to Medicaid programs. In an effort to be fiscally responsible for the state taxpayer dollars, State Medicaid Pharmacy programs, including TennCare, will prefer these significantly cheaper brand products that are the same as their generic counterparts to achieve additional savings to the program. Despite appearing more costly when dispensing in the pharmacy, TennCare, as well as other State Medicaid pharmacy programs, receive Federal Rebate dollars after dispensing making these brand agents much more cost effective for the program. Brand drugs that the TennCare pharmacy benefit prefers over the generic alternative will not require prior authorization for brand medically necessary (BMN), but may require clinical prior authorization. The branded agent may be submitted with a DAW code=5, substitution allowed, brand drug dispensed as generic for appropriate pharmacy reimbursement. These agents, although brand name, will have a generic copay for the patient and will either count as a generic agent towards the prescription limit or be considered exempt (if present on the Auto Exempt List). The list of brand agents preferred over generic counterparts are subject to change at any time due to availability of more cost-effective generic agents or changes in the marketplace. A current list of the plan preferred brand products can be found on the TennCare Pharmacy website at: https://www.optumrx.com/content/dam/openenrollment/pdfs/Tenncare/presciber/program-information/Brand%20as%20Generic%20List.pdf .

The articles in this issue of the TennCare Pharmacy Times were authored by:

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The content of this newsletter was approved by TennCare Pharmacy Unit.

TENNCARE IMPORTANT LINKS

The TennCare Medicaid fee-for-service Preferred Drug List (PDL) can be found at the following link: https://www.optumrx.com/content/dam/openenrollment/pdfs/Tenncare/presciber/clinical-criteria/Preferred%20Drug%20List%20(PDL).pdf

For more information about the TennCare Medicaid Pharmacy program, please access the following link: https://www.optumrx.com/oe_tenncare/landing

CONTACT US

TennCare Contact Information		
TennCare Member Services/Member Initiated Prior Authorization	**888-816-1680**	Available 24/7
Member Medical Appeals (formerly known as TSU)	**800-878-3192**	Available 24/7
Pharmacy Technical Call Center	**866-434-5520**	Available 24/7
Prescriber Prior Authorization	**866-434-5524**	Available 24/7
Prior Authorization Fax	**866-434-5523**	Available 24/7
TennCare Fraud and Abuse Hotline	**800-433-3982**	Available 24/7
Family Assistance Services Center	**866-311-4287**	Available 7am-5:30pm Monday-Friday
OptumRx/TennCare Provider Educators	**TNRxEducation@optum.com**	Available 8am-5pm Monday-Friday