

A Message to DMH Prescribers from Gerald Ko, Clinical Pharmacist

The DMH Pharmacy and Therapeutics committee has approved metformin for inclusion on PATS formulary as an adjunct to diet and lifestyle modifications in the management of antipsychotic induced metabolic adverse effects. Antipsychotic treatment has long been associated with weight gain, dyslipidemia, and blood glucose dysregulation both in literature and in clinical experience. Multiple studies have demonstrated metformin's efficacy in either minimizing therapy initiation associated weight gain or inducing weight loss for clients who have been stabilized on therapy (Maayan, et.al). In this brief bulletin we discuss DMH specific drug code information, recommended dosing, important monitoring guidelines, and DMH client specific cautions.

Metformin is available in 500 mg and 1000 mg strengths. The PATS drug codes for both products are MFN500 and MFN1000, respectively. The cost of treatment is estimated to be approximately \$10-\$15 per month per client. Please refer to the updated Drug Formulary link on <u>http://dmh.lacounty.gov/pharmacy</u> for full drug code information when entering in PATS. For non-indigent clients, metformin should be ordered via Orderconnect.

Recommended dosing for metformin is initially 500mg once daily with the evening meal, followed by weekly increase of 500mg until a maintenance dose of 1000mg twice a day is established. Metformin is has been demonstrated to be safe and well tolerated in long term (multiyear) treatment, with GI side effects (diarrhea, GI upset) being most prevalent (DPPR Group). Metformin has also demonstrated particular benefit to women in reversing antipsychotic associated amenorrhea (Wu, et. al).

A rare but important FDA Black Box Warning of lactic acidosis exists for metformin. Lactic acidosis is characterized by serum lactate levels of greater than 5 mmol/L and symptoms of deep rapid breathing, vomiting, and abdominal pain and is fatal in >50% of clients. This risk is further increased in renal impairment. It is therefore important to obtain a baseline serum creatinine (SCr) level for any client started on metformin therapy. Metformin should not be initiated in male clients with SCr of greater than 1.5 mg/dL and females with SCr levels of greater than 1.4 mg/dL. In addition, the risk of lactic acidosis increases with age and is exacerbated by alcohol use, as well as in clients concurrently on other medications with similar risk (ie., Nucleoside Reverse Transcriptase Inhibitors (NRTI's) in HIV clients). Therefore exercise caution when prescribing for the following types of clients:

*Geriatric clients

*HIV (check concurrent NRTI medications)

*Clients with suspected alcohol abuse or high alcohol intake

Clients should be counseled to recognize symptoms of lactic acidosis. In addition, clients should always be interviewed to ensure that metformin therapy is not concurrently prescribed by a physical health provider to prevent duplicate therapy. Should you have any questions or comments regarding this formulary update or would like to request additional references for information provided on this bulletin please do not hesitate to contact Pharmacy Services at (213) 738-4725.

Maayan L; Vakhrusheva J; Correll CU: Effectiveness of medications used to attenuate antipsychotic-related weight gain and metabolic abnormalities: a systematic review and meta-analysis. Neuropsychopharmacology 2010; 35:1520–1530

Diabetes Prevention Program Research Group: Long-term safety, tolerability, and weight loss associated with metformin in the Diabetes Prevention Program Outcomes Study. Diabetes Care 2012; 35:731–737

Wu R-R; Jin H; Gao K; Twamley EW; Ou J-J; Shao P; Wang J; Guo X-F; Davis JM; Chan PK; Zhao JP: Metformin for treatment of antipsychotic-induced amenorrhea and weight gain in women with first-episode schizophrenia: a double-blind, randomized, placebo-controlled study. Am J Psychiatry 2012; 169:813–821

To access previous bulletins, go to the DMH Pharmacy webpage: <u>http://dmh.lacounty.gov/wps/portal/dmh/clinical_tools/</u>

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