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Letter

Monitoring for post-injection delirium/sedation syndrome with long-acting olanzapine during the COVID-19 pandemic

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To the Editor

Olanzapine long-acting injectable (LAI), licensed in Australia for treatment of schizophrenia, improves medication adherence and prevents illness relapse (Kane et al., 2010). During premarketing clinical trials, in 0.07% of injections (Detke et al., 2010), olanzapine LAI administration was associated with post-injection delirium/sedation syndrome (PDSS). Symptoms and signs include acute sedation, delirium, slurred speech, ataxia and/or altered level of consciousness. It is caused by incidental injection into a venule during intramuscular administration. The median time to onset of initial signs and symptoms is 25 minutes (interquartile range, 12–60 minutes; Kane et al., 2010). Current monitoring guidelines recommend active monitoring of alertness every 30 minutes for 2 hours post-injection.

Given the current COVID-19 precautions, physical distancing requirements and resource constraints, 2-hour monitoring may not be feasible; however, cessation of olanzapine LAI is likely to lead to relapse of psychotic symptoms. Using publicly available data, we explored the post-marketing incidence of PDSS in Australian patients receiving olanzapine LAI, in order to assist in decision making around monitoring.

We included all 74,960 olanzapine LAI dispensings listed in the Pharmaceutical Benefits Schedule (PBS) database from the introduction of olanzapine LAI in January 2010 until the end of January 2020. Adverse event reports for all olanzapine formulations (and the subset of olanzapine LAI) were drawn from Australian Therapeutic Goods Association Database of Adverse Event Notifications (DAEN).

A total of 772 DAEN reports were related to all formulations of olanzapine, with 112 specifically linked to olanzapine LAI. All reports were reviewed for symptoms and signs associated with PDSS. For all formulations of olanzapine, rates of PDSS ranged from 0.03% of all injections when PDSS was specified in the DAEN report to 0.11% of all injections when all potential PDSS signs and symptoms were included (Table 1).

There are several caveats to interpreting this data. PBS can only provide dispensing data, which may be slightly

Table 1. Rates of post-injection delirium/sedation syndrome (PDSS).

	PDSS	Symptoms suggestive of PDSS[a]
All olanzapine formulations		
Number of unique events	23	80
Incidence rate	0.03%	0.11%
Olanzapine LAI formulation[b]		
Number of unique events	21	30
Incidence rate	0.03%	0.04%

LAI: long-acting injectable; DAEN: Database of Adverse Event Notifications.
[a]Symptoms suggestive of PDSS were assessed as any event listed in DAEN with at least one of the following terms: ataxia/gait disturbance, delirium, disorientation/confusional state, depressed level of consciousness/coma and dysarthia.
[b]The DAEN report specifically reports that olanzapine LAI was given.

higher than actual injections (Page et al., 2015). Only events per dispensing can be calculated, not events per patient. The PBS database does not capture any non-PBS subsidised prescriptions; however, this number is likely to be very low for LAI olanzapine. DAEN is a voluntary database and although most serious adverse events such as PDSS are usually reported to DAEN, it may not capture all events.

These data suggest that PDSS following olanzapine LAI injection is rare. The benefits of continuing access to a medication that reduces risk of relapse and decreases time in patient waiting rooms with their associated risk of exposure to infectious disease may outweigh the risk of developing PDSS. In situations where 2-hour monitoring is unsafe or unfeasible, it may be worth considering reducing the monitoring period to 30 minutes to an hour, or temporarily removing the clinical staff monitoring requirement for appropriate patients who have a responsible person to assist in supervision post-injection.

Declaration of Conflicting Interests

D.S. and K.N. have no conflicts of interest to declare. M.B. has had interactions in the last 5 years with Janssen-Cilag, Allergan, Astra Zeneca, Bioadvantex, Bionomics, Collaborative Medicinal Development, Grunbiotics, LivaNova, Lundbeck, Merck, Mylan, Otsuka and Servier. D.C. has received grant monies for research from Eli Lilly, Janssen-Cilag, Roche, Allergen, Bristol-Myers Squibb, Pfizer, Lundbeck, Astra Zeneca and Hospira; travel support and honoraria for talks and consultancy from Eli Lilly, Bristol-Myers Squibb, Astra Zeneca, Lundbeck, Janssen-Cilag, Pfizer, Organon, Sanofi-Aventis, Wyeth, Hospira and Servier; and is a current Advisory Board Member for Lu AA21004: Lundbeck; Varenicline: Pfizer; Asenapine: Lundbeck; Aripiprazole LAI: Lundbeck; Lisdexamfetamine: Shire; and Lurasidone: Servier. He has no stocks or shares in any pharmaceutical company. C.G. had had clinical trials funded by Bristol-Myers Squibb Research & Development, Janssen Research & Development, ICON Clinical Research P/L, Envivo Pharmaceuticals/INC Research, and has received professional fees from Lundbeck and Janssen-Cilag. A.H. has received consultancy fees from Janssen Australia and Lundbeck Australia. He has been on an advisory board for Sumitomo Dainippon Pharma. He has received payments for educational sessions run for Janssen Australia and Lundbeck Australia. He has developed educational material for Servier. He is also the recipient of an investigator-initiated grant from Takeda Pharmaceutical Company.

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