

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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Palliative Care Pharmacy Team:

Clinical Pharmacy Specialist:

**Maria Felton Lowry, PharmD, BCPS, BCGP**  
Assistant Professor  
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics  
Palliative Care Clinical Pharmacy Specialist  
UPMC Palliative and Supportive Institute

Cell: 412-627-8473  
Office: 412-864-2899  
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

## TODAY'S TOPIC:

### Antipsychotic Adverse Drug Reactions: Focus on QTc Prolongation

#### Background:

Antipsychotics have been used for many years to treat mental health conditions. Generally, antipsychotics reduce dopamine neurotransmission. First-generation antipsychotics and second-generation antipsychotics differ with their degree of blockade of other neurotransmitters that can be helpful for palliation of a variety of symptoms.

#### Importance:

Antipsychotics can cause QTc prolongation. As stated last week: clinically significant QTc prolongation is an absolute QTc  $\geq 500$  msec, QTc  $\geq 25\%$  from baseline, or change of QTc  $\geq 60$  msec.<sup>1</sup> The degree of QTc prolongation is a *modest* predictor of the risk of Torsades de Pointes (TdP) and sudden cardiac death.<sup>2</sup> Still, it is important for palliative care clinicians be aware of this risk of commonly prescribed medications in our practice.

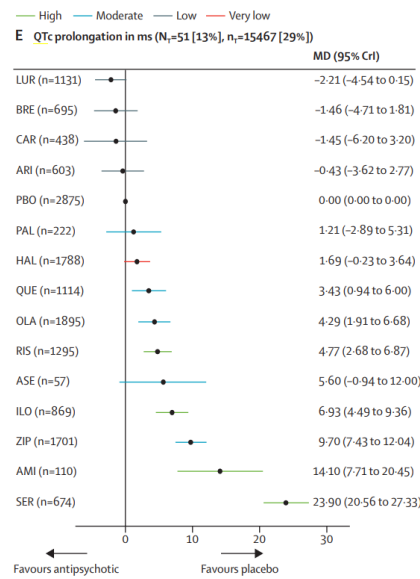
#### Known QTc prolongation risk factors:

- Age  $\geq 65$
- Female
- Electrolyte imbalances: hypokalemia, hypomagnesemia, hypocalcemia
- Impaired hepatic and/or renal function
- Cardiovascular Disease (CHF, AFib, MI)
- Medications: Methadone, Tyrosine Kinase Inhibitors (Crizotinib, Sunitinib, Vemurafenib, Sorafenib, Imatinib), SSRIs, Fluoroquinolones, Amiodarone, Antiemetics
- Drug interactions: inhibition of cytochrome P450 enzyme and subsequent increase in medication plasma levels (Antifungals, Macrolide antibiotics, ritonavir, verapamil, St. Johns Wart)

#### The Literature:

[Lancet. 2019 Sept 14;394\(10202\):939-951.](#)

**Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis**  
Meta-analysis (n=15,467 for QTc prolongation outcome)



AMI=amisulpride  
ARI=aripiprazole  
ASE=asenapine  
BRE=brexipiprazole  
CAR=cariprazine  
HAL=haloperidol  
ILO=iloperidone  
LUR=lurasidone  
OLA=olanzapine  
PAL=paliperidone  
PBO=placebo  
QUE=quetiapine  
RIS=risperidone  
SER=sertindole  
ZIP=ziprasidone

[Psychosomatics. Jan-Feb 2013;54\(1\):1-13.](#)

#### QTc prolongation, torsades de pointes, and Psychotropic medications

Literature Review

[Curr Psych. 2012 Oct;11\(10\):36-39.](#)

#### Which psychotropics carry the greatest risk of QTc prolongation?

Commentary

Data extrapolated from Psychosomatics and Curr Psych articles:

Antipsychotic	Approximate QTc interval prolongation (msec)*a	Association with TdP
Aripiprazole	-1 to -4	-
Haloperidol	7 to 15	+++ (IV) ++ (PO/IM)
Olanzapine	2 to 6.5	+
Quetiapine	6 to 15	+
Risperidone	3.5 to 10	+
Thioridazine	33 to 41	+++
Ziprasidone	16 to 21	+

\*This is dependent on dose as well as route of administration (IV > PO)

a Ranges may seem smaller than we see in clinical practice given complexity of our patients

[J Psychiatr Pract. 2014 May;20\(3\):196-206.](#)

#### QTc prolongation with antipsychotics: is routine ECG monitoring recommended?

Literature Review

ECG monitoring	Antipsychotics
Recommended. Do not use in patients with increased cardiac risk.	Thioridazine, droperidol, haloperidol(IV) > 2mg cumulative dose
Recommended in presence of risk factors. Keep low threshold for cardiac risk status on initial eval.	Ziprasidone, Chlorpromazine, Haloperidol (PO), Quetiapine
Recommended in presence of risk factors.	Aripiprazole, Clozapine, Olanzapine, Paliperidone, Risperidone

#### Bottom Line:

- Literature on degree of QTc prolongation for each antipsychotic differs slightly, however consistently ziprasidone and thioridazine are deemed high risk, and not used often in PC.
- Degree of QTc prolongation is likely related to cumulative dose and higher with IV route of administration, this is including haloperidol, which we use often in our clinical practice.
- Degree of QTc prolongation does not equate to risk of TdP.
- Routine ECG monitoring is not recommended unless planning to utilize "high risk" antipsychotic and patient has underlying risk factors.
- Although not much data exists surrounding aripiprazole use in PC, might be worth trying if patients have multiple risk factors for QTc prolongation.

1. Ann Noninvasiv Electrocardiol. 2020;25:e12699.  
2. CNS Drugs. 2014 Oct;28(10):887-920.

#### CLINICAL PEARL:

Recommend using lowest effective dose of antipsychotic possible, being mindful of coadministration with other QTc-prolonging medications, as well as other comorbidities/risk factors.