

## **Typical antipsychotics (conventional) (FGA)**

**Treats positive (+) symptoms only appropriate for the acute and chronic**

**management of schizophrenia and psychosis.**

**Non-selectively blocks dopamine D2 receptors, specifically in mesolimbic pathway;**

**also blocks Ach (Muscarinic), histamine, NE**

**Five main SE of FGAs**

- . Sedation
- . Postural Hypotension
- . Lower seizure threshold
- . Anticholinergic side effects
- . Photosensitive

**Haloperidol**-High-Appropriate for acute, severe agitation and aggression-Butyrophenones

- . Initial oral dose 1-15mg/day (can give once daily or divide);
- . Usual dose 1-40mg/day (orally);
- . Max dose 100mg/day
- . Tablets 0.5, 1, 2, 5, 10, 20mg; Concentrate 2mg/ml; Injection 5mg/ml
- . Half-life 13-38
- . Higher risk for EPS and TD
- . **Avoid in older adults** due to increased risk of cerebrovascular accident (CVA), cognitive decline, and death in persons with dementia and with dementia-related psychosis.

**Fluphenazine**-Medium-Psychotic D/Os

- . Initial oral dose 0.5-10mg/day divided doses;
- . Usual dose 1-20mg day;
- . Max dose 40mg/day
- . Tablet 1, 2.5, 5, 10mg; Elixer 2.5mg/ml; Concentrate 5mg/ml
- . Half-life 15 hours

**Thiothixene**-Medium

- . Initial dose 5-10mg/day;
- . Usual dose 15-30mg/day;
- . Max dose 60mg/day divided
- . Capsules 2, 5, 10mg
- . Half-life 3.4-34 hours

**Thioridazine**-Low-2<sup>nd</sup> line due to QTc issues

- . Initial dose 50-100mg/3xday/increase gradually;
- . Usual dose 200-800mg divided;
- . Max dose 800mg/day
- . Tablets 10, 15, 25, 50, 100mg
- . Metabolized by CYP450 2D6

**Chlorpromazine**-Low-2<sup>nd</sup> line due to QTc issues -schizophrenia-DA 2 antagonist

- . Usual dose 200-800mg divided; maximum 800mg/day
- . Psychosis-increase dose until symptoms are controlled; after 2 weeks reduce to lowest effective dose
- . Can improve in one week but may take several weeks for full effect on behavior

- . Tablet 10, 25, 50, 100, 200mg
- . Half-Life 8-33 hours
- . Phenothiazine
- . SXS-Dry mouth, pupil dilation, blurred vision, cog impair, constipation, urinary retention, tachycardia

**Mesoridazine**-Low-off market due to dangerous side effects, including irregular heartbeat and QT prolongation.

\*Low potency meds require higher doses to achieve efficacy

\*Low potency meds have more anticholinergic, antihistaminic, and a 1 properties resulting in more sedation than higher potency meds.

\*High risk for developing hyperprolactinemia and EPS (negative symptoms aren't affected by FGAs only positive symptoms)

**Neuroleptosis** is a term to describe antipsychotic medication effects on psychotic clients, with respect to cognition and behavior. Newer medications (SGA) do not necessarily have these same effects.

**Neuroleptosis syndrome** has three major features. Examine the image below to learn more about the PEA acronym.

- . **Psychomotor slowing** - extreme form of slowness or absence of motor movement (nigrostriatal pathway)

- . **Emotional quieting** - worsening of negative and cognitive symptoms (mesocortical pathways)

- . **Affective indifference** - worsening of affective symptoms (mesocortical pathway)

**Atypical antipsychotics (SGA) Developed to treat both positive (+) and (-) negative symptoms**

- . SGAs are considered serotonin-dopamine antagonists, as they maintain D2 antagonism but also have simultaneous serotonin 5HT<sub>2A</sub> antagonism

- . Lower affinity for D<sub>2</sub> and higher affinity for 5HT

- . Effective for treatment-resistant clients

- . Does not increase prolactin levels

- . Treats positive and negative symptoms

- . Lower risk of EPS

**Olanzapine**-Schizophrenia- age 13 and older

- . Serotonin-Dopamine antagonist-reducing positive sx's; Antagonist actions at the 5HT<sub>2C</sub> receptor may contribute to efficacy for cognitive and affective sx's

- . \*More weight gain and metabolic effects

- . \*High metabolic risk

- . Highest risk for weight gain, blood dyscrasias, QT prolongation, cardiovascular disease, cerebrovascular effects, hyperglycemia, and \*hyperprolactinemia

- . Most commonly used in pregnant women with least risk for congenital harm

- . Half-life 21-54 hours

- . Substrate for CYP450 1A<sub>2</sub> and 2D<sub>6</sub>

- . Usual dose 1-20mg/d

- . Initial dose 5-10mg/d increase by 5mg/day once a week until desired efficacy

- . Max dose 20mg/d
- . MOA-
- . Special Comments: Best tolerated antipsychotic
- . **AVOID IN PREGNANCY!**
- . **Avoid in older adults** due to increased risk of cerebrovascular accident (CVA), cognitive decline, and death in persons with dementia and with dementia-related psychosis.

**Quetiapine**-Acute schizophrenia in adults and aged 13-17

- . Serotonin-Dopamine antagonist, also a mood stabilizer
- . Most commonly used in pregnant women with least risk for congenital harm
- . Usual dose 400-800mg divided; maximum 800mg/day
- . Initial dose 25mg/BID, increase by 25-50 twice a day until efficacy reached
- . Tablet 25, 50, 100, 150, 200, 300, 400mg
- . Half-Life 6-7 hours
- . Substrate for CYP450 3A4
- . MOA-
- . Moderate metabolic risk
- . Low EPS risk
- . Risk of orthostatic hypotension, blood dyscrasias (neutropenia, leukopenia, and agranulocytosis), QT prolongation, weight gain, and renal and hepatic impairment
- . **AVOID IN PREGNANCY!**
- . **BLACK BOX WARNING: Increased risk of suicidal ideation and suicidal behavior in adolescents/young adults during the initial 1-2 months of treatment**
- . **CAUTION: exercise caution in suspected alcohol withdrawal, stimulant intoxication, or anticholinergic intoxication**

**Asenapine**-Schizophrenia adults and kids 10 and older

- . Serotonin-Dopamine antagonist
- . Blocks DA2 receptors reducing positive sxs and stabilizing affective sxs
- . Blocks 5HT2A receptors causing enhancement of DA release in the brain and reduces motor side effects and possibly improves cog and affective sxs
- . MOA.

Special Comments: \*Available in sublingual and transdermal patch

- . Risk: Low metabolic risk

**Clozapine**-Treatment resistant schizophrenia; reduction of risk of recurrent suicidal behavior in

pts with schizo; Not indicated in acute presentation of schizophrenia

- . Serotonin-Dopamine antagonist, also a mood stabilizer
- . Fewer EPS than FGAs 2/2 reduced D2 receptor affinity
- . \*Tx Resistant SP
- . Little to no sxs of movement d/o
- . **AVOID IN PREGNANCY!**
- . Toxic effect on WBC...ANC must be >1500/mm<sup>3</sup>...NEEDS INITIAL AND WEEKLY MONITORING OF WBC, GRANULOCYTE, and NEUTROPHIL COUNTS

- . MOA-Blocks DA2 receptor reducing (+) sx; Blocks 5HT2A receptors causing enhancement of dopamine release in certain brain regions and thus reducing motor side effects and possibly improving cognitive and affective sx
- . SE- Weight gain issue, sedation, sialorrhea, agranulosis (WBC decrease), lowered seizure threshold High metabolic risk
- . Highest risk for weight gain.
- . Low EPS risk.
- . Black box warning: may cause severe neutropenia
- . Contraindicated in liver disease and hepatic failure
- . Not a first-choice medication for treating schizophrenia

### **Risperidone**-Schizophrenia ages 13-adults

- . Usual Dose 2-8mg/d for acute psychosis
- . Max Dose 16mg/d
- . Initial dose 1mg/d in 2 divided doses increase each day by 1mg until efficacy reached
- . Metabolized by CYP450 2D6
- . Half-life 20-24 hours
- . Notable side effects: metabolic syndrome, dose dependent drug induced parkinsonism, \*\*\*\*\*Hyperprolactinemia\*\*\*\*\*
- . Serotonin-Dopamine Antagonist
- . Most commonly used in pregnant women with least risk for congenital harm
- . MOA-
- . Moderate metabolic risk
- . Risk of blood dyscrasias, QT prolongation, cardiovascular, and cerebrovascular effects
- . **AVOID IN PREGNANCY!**

### **Paliperidone**-Schizophrenia 12 and older

- . MOA
- . SE
- . Serotonin-Dopamine antagonist

### **Ziprasidone**(Geodon)-Schizophrenia 10 and older

- . MOA-
- . SE-moderate metabolic risk
- . Serotonin-Dopamine antagonist
- . Special Comments: IM dosing in acute agitation associated with schizophrenia
- . Low metabolic risk
- . Lowest risk for weight gain
- . **AVOID IN PREGNANCY!**
- . **Avoid in older adults** due to increased risk of cerebrovascular accident (CVA), cognitive decline, and death in persons with dementia and with dementia-related psychosis.
- . Contraindicated in clients with QT, recent myocardial infarction, or uncompensated heart failure
- . High incidence of rash/urticaria related to Stevens-Johnson syndrome and Drug Reaction with Eosinophilia and Systemic Syndrome (DRESS)

### **lloperidone**-Schizophrenia; Schizophrenia maintenance

- . Usual dose 12-24mg /d (divided in two)
- . Max dose is 32mg/d

- . Max dose is 16mg/d for those who are poor 2D6 metabolizer
- . If prescribed with a CYP 3A4 inhibitor dose should be 8mg/d
- . MOA-
- . Moderate risk for weight gain
- . Low risk for hyperlipidemia

**Lurasidone**-(latuda)Schizophrenia 13 and older

- . MOA
- . SE-low metabolic risk
- . Serotonin-Dopamine antagonist
- . TAKE WITH FOOD, AT LEAST 350 CALORIES FOR MAX ABSORPTION
- . Blocks DA2 receptors reducing (+) sx's of psychosis and stabilizing affective symptoms;
- . Blocks 5HT2A receptors causing enhancement of dopamine release in certain brain regions and thus reducing motor side effects and possibly improving cognitive and affective sx's

**Aripiprazole**-(Abilify)Schizophrenia 13 and older

- . Listed as SGA or TGA
- . partial agonist at D2, 5HT1a, 5HT2
- . When DA levels are high it reduces DA output improving positive sx's
- . When DA levels are low it increases DA output improving negative sx's, mood and cog
- . Usual dose 15-30mg/d for SP and mania
- . Initial dose 10-15mg/d
- . Max dose 30mg/d
- . Max dose is 15mg/d for those who are poor 2D6 metabolizer
- . If prescribed with a CYP 3A4 inhibitor dose should be 7.5mg/d
- . MOA
- . Low metabolic risk
- . Low risk for weight gain
- . Low risk for orthostatic hypotension
- . BLACK BOX WARNING: Increased risk of suicide in children.

**Brexpiprazole**-(Rexulti) AKA a (TGA)-Schizophrenia

- . Usual dose 2-4mg /d
- . Max dose is 4mg/d
- . Max dose is 2mg/d for those who are poor 2D6 metabolizer
- . If prescribed with a CYP 3A4 inhibitor dose should be 1mg/d
- . MOA-Partial agonism at dopamine 2 receptors
- . SE-Low metabolic risk
- . Special Comments: Considered precognitive
- . Dopamine-Serotonin Partial Agonist

**Cariprazine** (Vraylar)-schizophrenia

- . MOA
- . SE Low Metabolic risk

\*Order fasting Glucose, Lipids, EKG, BMI, BP when on SGAs

**Prescribing Considerations**

1. Start with the lowest dose, evaluate tolerance, then slowly titrate dose to efficacy. Titrating helps prevent undesirable side effects.
2. There is no evidence that high antipsychotic doses are more effective than standard doses.