

# MEDICAL MEMO

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## "Antipsychotic" Medicines

Antipsychotic medications were invented in the 1950's to treat psychosis. Psychosis means "out of touch with reality" and typically includes hallucinations, delusions, and severe, bizarre, or very paranoid, thinking known as "thought disorder". Generally people experiencing psychosis have schizophrenia, psychotic depression, or bipolar disorder (manic depression), but may have drug or medicine abuse, toxicity, or withdrawal, may be reacting to a catastrophe (brief reactive psychosis) or may have a brain injury or disorder like dementia or delirium, or other health conditions.

Antipsychotics, like other medicines, may help other conditions as well. Used alone or in combination with other treatments, antipsychotics are effective for nausea and vomiting (e.g. Compazine), are good sedatives, help sleep, calm agitation and irritability, help impulsive aggression, treat the tics of Tourette's syndrome, help behavioral problems associated with head injuries, and help some symptoms of Autistic Spectrum Disorder (ASD). Antipsychotics are sometimes used as boosters to make other medicines more effective in Obsessive Compulsive Disorder (OCD), Depression, severe Anxiety, and other conditions where thinking, compulsive or impulsive behaviors are problems. The "atypical" antipsychotics also work as mood stabilizers. They are usually the best treatments for mania and are often good for acute depression. They also show promise in lessening recurrence of both mania and depression like the classic mood stabilizers lithium, Depakote (valproic acid, divalproex), Tegretol (carbamazepine), and Lamictal (lamotrigine).

**The "atypicals" are Clozaril (clozapine), Risperdal (risperidone), Zyprexa (olanzapine), Seroquel (quetiapine), Geodon (ziprasidone), Abilify (ariprazole), Invega (paliperidone) plus the newest three – Saphris (asenapine), Fanapt (iloperidone) and Latuda (Lurasidone).** Clozaril is used least despite potential excellent benefits and no Tardive

Dyskinesia risk because of its complex side effect profile.

There are two main groups of antipsychotics - typical and atypical. Atypical means not typical. All antipsychotics decrease action of the neurotransmitter dopamine in the brain (dopamine blockers). Atypical antipsychotics (called "atypicals" for short) also partly decrease the action of serotonin. This double, or dual, action gives atypicals their broader benefit and changes their side effect patterns, mostly for the better.

[My medicine chart on Antipsychotics, page 1](#), gives useful information about the Typical antipsychotic group including names, doses, common side effects, pros, and cautions. Some common and useful typicals, all available as generics, include Haldol, Orap (pimozide - often the best for tics) and several others.

[The medicine chart Antipsychotics, page 2](#) provides information about the **Atypical antipsychotic group**. Atypicals are newer, have are still under patent (except Risperdal, Seroquel, Geodon, Zyprexa, and Clozaril; all of which have generics), and thus often much more expensive than the typicals. Atypicals are usually preferred due to their generally broader benefits and substantially reduced rate of short and long term "extrapyramidal" side effects. Another advantage of the atypicals, unlike typicals, is they help not only the obvious schizophrenia symptoms of hallucinations, delusions, and severe thought disorder but also better reduce so called "negative" symptoms of schizophrenia like apathy, poor motivation, and alienation from society and also help stabilize mood. Unfortunately, atypicals (except Geodon and perhaps Latuda) often cause weight gain, may increase diabetes, cholesterol, triglyceride, and blood pressure.

**The two main advantages of the Atypicals over the Typicals is the broader range of diagnoses and symptoms they treat and their substantially reduced risk of causing extrapyramidal symptom (EPS) side**

**effects.** Short term reversible EPS include parkinsonian symptoms (looks like but isn't Parkinson's disease), akathisia (internal restlessness), acute dystonic reactions (scary, often sudden onset, intense muscle tightness/cramp like but brief and often easily treated), and related effects. These short term reversible EPS side effects can be reduced or prevented by changing the antipsychotic medicine dose, changing the antipsychotic medicine to a different one, stopping the antipsychotic, or adding a medicine like benztropine, benadryl, amantadine or a beta blocker to counteract the EPS.

Tardive Dyskinesia (TD) is a possibly irreversible EPS movement disorder long term side effect. The primary risk is from long term (usually years, rarely less than six months), high dose treatment with the older typical antipsychotics that are also known as neuroleptics. The risk of TD is close to (but not) zero for low dose short term (weeks to months) use. The risk of TD with the old "Typical" group is about 1 to 5% per year (this means about 1 to 5 of every 100 persons who takes an average dose of one of these medicines for a year will show some TD at the end of that year). The newer atypical antipsychotics have a much lower risk, estimated at roughly 0.1% to 0.5% per year (1 to 5 in 1000 will show TD after a year). Risperdal, Abilify and Geodon are probably close to the 0.5% risk while Seroquel and Zyprexa, are at the 0.1% level. The other atypicals' TD risk are between 0.1 and 0.5%. Clozaril treats or even reverses TD. Antidepressants, anti-anxiety meds, sleeping meds, mood stabilizers, and stimulants do not carry any TD risk at all. Tardive Dyskinesia (TD) is a group of abnormal movements that typically start mildly with subtle involuntary snake like (choreo-athetoid) and/or chewing-like frequent movements of the tongue and mouth and may progress, especially with continued use of the medicine, to affect the arms, legs, and other parts of the body in severe cases. TD may be very mild to severe and disabling with the degree usually related to the dose and duration of antipsychotic medicine exposure. TD symptoms are not always caused by medication. Abnormal movements indistinguishable from TD occur in some people with other neurologic conditions, some people with schizophrenia, and even in some elderly persons, even without any treatment ever with an antipsychotic medicine. About 1/3 of TD cases believed to be caused by antipsychotic medication recover completely with or without any special treatment other than stopping the antipsychotic, if possible. Another 1/3 improve with time and treatment but not fully. The final 1/3 do not improve or recover and may worsen even to

disability. The best treatment for TD is using Clozaril although other options exist but are less consistently helpful or are experimental. **Prevention of TD is the best treatment.** My patients who take the antipsychotics become used to the modified AIMS testing I do at some of our follow-up visits. They are most aware of the finger tapping and tongue examination but are less aware of the way I watch them walk, sit, stand, and how I look for other subtle early signs of Tardive Dyskinesia. I am also watching and listening for signs of the reversible and treatable false parkinsonian, acute dystonia, and akathisia symptoms.

Neuroleptic Malignant Syndrome (NMS) is a rare but potentially dangerous hypersensitivity reaction that is fortunately rare with atypicals, especially at lower doses. The greatly reduced risk of all EPS, especially TD and NMS, is a big advantage of the atypicals and makes these medicines feasible for more patients with far less risks than with the older "typicals".

**Zyprexa (olanzapine)** may be the most effective (other than clozapine) but has relatively high sedation and weight gain. It also has the lowest EPS risk, next to its cousin clozapine. **Risperdal** has been used the most in kids and is FDA approved for Autism (as is Abilify). **Seroquel** is an alternative with moderate to strong sedation (sleep help), low EPS risk, and mid-range weight gain risk. **Geodon** has variable sedation, mid EPS risk, and no weight gain (this is a big plus in its favor). Geodon has a tendency to mildly slow heart conduction but this is rarely a problem and especially not at lower doses (checking an EKG may be useful if heart symptoms or high dose). **Invega** is an extended release atypical related to Risperdal. **Saphris, Latuda** and **Abilify** are moderate re weight gain, EPS (movement disorder side effects) and sedation. **Fanapt** has little to no EPS effects (clozapine has none). No atypicals (except clozapine) require regular blood or other special testing and generally are easy to give. Geodon comes only in capsules. Saphris is taken under the tongue (sublingual). Risperidone is the most likely to increase the hormone prolactin. Latuda along with Seroquel (quetiapine), Zyprexa (olanzapine), risperidone, and Abilify (ariprazole) can make antidepressants work better and are good for Bipolar Depression.

**Metabolic side effects** refer to the medication causing or increasing risks for weight gain, higher blood pressure, higher cholesterol and triglycerides (lipids), higher blood sugar, and higher risk of diabetes. Whether this occurs due to medicine increasing appetite and thereby weight

or by directly worsening metabolism even without weight gain is unresolved. My impression is that the primary concern and underlying mechanism is increased appetite and thus weight gain. This is why I often prefer ziprasidone (Geodon) or Latuda as a first choice.

Once daily dosing is common for all antipsychotics although sometimes twice or more doses a day are given for smoother effects. All work rapidly, often in the first few days or first week. I have seen many situations where an atypical antipsychotic medicine has rapidly stopped a potentially dangerous situation that might have otherwise gone on to hospitalization, arrest, or serious harm.

**So which is best?** As usual, that depends on matching the medicine to the patient, the target symptoms, diagnosis, what has been tried before, history of response to other treatments, cost, whether a split-able pill or liquid needed, what effects are wanted, what effects are not wanted, and whether even the side effect might be a benefit for this person.

**In summary**, although we still need more and better medicines and other therapies, the atypical antipsychotics are welcome additions to our treatment options. They are often rapidly helpful in crisis situations where other lesser options have failed. I particularly like them for severe impulsive aggression and rage or as boosters when other treatments have been inadequate. Low to moderate doses are usually enough. They are quite safe and easy to use. Although the risk of Tardive Dyskinesia makes them “big guns” the risk of TD is low, especially on a short term basis. They are also easier and safer to use than other “big guns” like Tegretol (carbamazepine), Depakote (divalproex), Lithium, and the older typical antipsychotics. It is important to remember that we don’t often use antipsychotic medicine for aggression unless the situation is severe, other therapy and medicine attempts have failed, and the med usually won’t be kept unless it is very helpful. Then we can decide how long to keep them and what else to do at a more comfortable pace after the crisis is past.

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