POLYPHARMACY JUSTIFICATION CHECKLIST

	YES	NO
1. Before prescribing polypharmacy:		
a. Thorough evaluation of clinical presentation?	☐	☐
b. Thorough evaluation of diagnosis?	☐	☐
2. Evaluation of medication history:		
a. Efficacy of past medications documented/reviewed?	☐	☐
b. Reported side effects of past medications documented/reviewed?	☐	☐
c. Dose and duration of past monotherapy attempts documented/reviewed?	☐	☐
i. At least 21 days of continuous use at same dose? (Mood stabilizers and antipsychotics may require longer trials.)	☐	☐
ii. 2-to-3 monotherapy trials with drugs from different classes?	☐	☐
iii. Review of diagnosis after failure of several monotherapy trials?	☐	☐
3. Patient compliance:		
a. Review of patient compliance during medication trial(s) documented?	☐	☐
b. Patient involvement in reviewing treatment response and treatment options?	☐	☐
c. Review of simplicity of regimen and avoiding complicated regimen?	☐	☐
4. Evaluation of the current medication regimen:		
a. Rationale for each current medication reviewed?	☐	☐
b. Efficacy of each current medication reviewed?	☐	☐
c. OTC medications, herbal remedies, and illicit drugs reviewed?	☐	☐
d. One-time orders and prn medications reviewed? (If >3/week for 3-4 weeks, these should be considered part of a patient's scheduled medication regimen).	☐	☐
5. Review of medication changes:		
a. Total number of medications reduced before adding new one?	☐	☐
b. Only one medication changed at a time?	☐	☐
c. Medication changes completed? Old medication discontinued after new one at therapeutic level for sufficient period of time?	☐	☐
d. Cross-titrations used only with those medications for which this strategy is required?	☐	☐
6. Demonstrable need:		
a. Medications without clear benefit for target symptoms eliminated?	☐	☐
7. Combined and Augmented Pharmacotherapy:		
a. Justification for same-class polypharmacy clearly documented?	☐	☐
i. Specific targeting of different symptom clusters?	☐	☐
ii. Synergism in the drugs' mechanisms of action?	☐	☐
iii. Augmentation of partial treatment response or nonresponse to monotherapy?	☐	☐
iv. Improved risk/benefit ratio by reducing dosage and adverse effects for improved tolerability of one or both drugs?	☐	☐
b. Failed trials of monotherapy documented?	☐	☐
c. Efficacy data on strategically combined treatments reviewed?	☐	☐
8. Monitoring the risks of polypharmacy:		
a. Drug interactions reviewed?	☐	☐
b. Blood levels monitored periodically, especially with signs of toxicity or with medications likely to have drug interactions?	☐	☐
c. Monitoring of higher-risk combinations:		
i. More than one medication from the same class?	☐	☐
ii. More than two antipsychotic medications?	☐	☐
iii. Combinations with cumulative anticholinergic effects?	☐	☐
iv. Combinations with specific additive organ or system effects? (e.g., Cardiac, Renal, Hepatic, Respiratory, Gastrointestinal, Musculoskeletal)	☐	☐
9. Institutional mechanisms in place:		
a. Peer review	☐	☐
b. Automatic/forced drug interaction reviews	☐	☐
c. Supported access to medication information	☐	☐
d. Pharmacy consultation	☐	☐
e. Drug utilization review	☐	☐

Background Information

Polypharmacy has a number of definitions, including more than one drug for a single patient, more than one drug for a target symptom, and more than one drug from the same class. The most common reasons for polypharmacy are monotherapy has been ineffective, aggressive targeting of specific symptoms, treating distinct but co-morbid conditions, treating refractory symptoms, and treating side effects of a primary drug. Psychiatric pharmacotherapy is thought to occur more frequently than is supported by research data. 25-50% of patients in psychiatric treatment are prescribed more than one antipsychotic agent, and the prevalence of add-on, augmenting, or adjunctive (treating side effects of another drug) pharmacotherapy is 28-75%.

Up to 85% of physicians have been reported as prescribing more than one antipsychotic to refractory patients. This includes both the temporary use of multiple medications and medications used in cross-titrations. Up to 80% of patients get caught in the "crossover trap," while switching from one medication to another. Usually, the level of improvement while on medications made the patient or physician unwilling to go ahead and complete the crossover. Generally speaking, research has not supported these clinician or patient perceptions that combination antipsychotic therapy is more effective than monotherapy, and many suggest that a cross-titration may be unnecessary for atypicals.

There are few studies evaluating efficacy, risk, and long-term effects of polypharmacy. Combinations of two drugs have shown efficacy in the treatment of a number of psychiatric disorders, including bipolar disorder, severe or refractory depression, schizoaffective disorder, and schizophrenia with prominent depression. Combinations of more than 2 drugs are not well supported by scientific research, beyond the combined use of mood stabilizers, antipsychotics, and anxiolytics in acute mania. Same-class polypharmacy should be rare in general psychiatry, but in our target populations, it will not be rare. We must take on the responsibility for advocating for patients when monotherapy has failed and we have evidence for enhanced efficacy with combined treatment; to do so requires careful documentation, an acknowledgement of the general need to avoid polypharmacy, and clear justification for the combined or augmented treatment.

Factors associated with polypharmacy include sicker, more disabled patients; repeated hospitalizations within one year; younger age; male; involuntary commitment or MOT; and a diagnosis of schizophrenia, bipolar disorder, or mania. Drug interactions become much more significant in medication management, and include alterations in the nature, magnitude, and duration of drug effects; absorption, distribution, metabolism, and excretion; additive adverse effects; and both increases and decreases in desired effects. Sicker patients not only get multiple medications, but also medications at higher doses, increasing the risks of drug toxicity when using multiple medications at maximum dosages. Polypharmacy poses additional risks in pharmacotherapy, including more adverse drug reactions, more severe adverse drug reactions, more drug interactions, more cumulative toxicity, more medication errors, more patient noncompliance, and more patient morbidity and mortality. The likelihood of death is directly proportional to the number of medications prescribed, even when controlled for the underlying disorder(s).

Specific polypharmacy in treatment-resistant conditions is a community standard that should be supported by assessment of the clinical presentation and by the medical literature. Combinations generally thought to be without justification include:

- Drugs from the same class to treat the same symptoms, with specific reference to typical antipsychotics; benzodiazepines, tricyclics, SSRIs, MAOIs, or other antidepressants from the same class; and stimulants.
- Use of more than two antipsychotics, typical or atypical.
- Change in dose before steady state and sufficient time for therapeutic response.
- Failure to adequately evaluate and monitor patients who are receiving polypharmacy.

Recommendations arising from reviews of poor outcomes in polypharmacy:

- Thoroughly evaluate the patient's symptoms and medication regimen.
- Refrain from polypharmacy when possible; plan carefully and monitor response when it must be done.
- Only prescribe that for which there is a demonstrated need.
- Avoid using combinations from the same class of medication to treat the same symptoms.
- Consider drug interactions.
- Be familiar with adverse drug effects and how they are manifested in the patient.
- Carefully monitor for adverse drug effects, including cumulative anticholinergic effects.
- Obtain drug levels if applicable.
- Arrange for adequate follow-up.
- Arrange for general medical evaluation, especially if the patient appears medically ill and the deterioration is no clearly consistent with the psychiatric diagnosis.

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