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Evidence-based Best Practices for the Treatment of Schizophrenia in South Carolina

Schizophrenia is a challenging illness for both clinicians and patients who often require a lifetime of treatment. The SCORxE schizophrenia algorithm offers state providers unbiased, evidence-based clinical information about drug therapy and best practices to assist with making best prescription decisions.

Use an adequate trial of an antipsychotic, consisting of BOTH an adequate medication dosage and duration.

- A minimum of 4 weeks of therapeutic doses of an antipsychotic (except clozapine which requires up to 3 months) is needed before non-response to that medication can be established.
- Assessing the full effects of an antipsychotic can take 12 weeks or longer.
- When a patient who has been stable on antipsychotic medication has an acute exacerbation, a change in medication may not be necessary. Often the exacerbation is due to nonadherence (e.g., substance abuse, environment, or social stressors).

Use a rating scale to assess symptom severity before initiating medication; then repeat scale at regular intervals to assess patient response and determine if further dose adjustments are needed.

- Assess core symptom severity and other symptoms (e.g., anxiety, mood lability).
- Administer brief positive and negative rating scales.
- Obtain a global report of symptoms and side effects from patients.

Talk with the patient and family about the importance of medication adherence and collaborate to provide symptom relief and minimize side effects.

- Weekly monitoring of compliance and side effects is recommended during an acute episode.
- When possible, avoid changing antipsychotics after only minimal side effects.
- Allow 4 to 6 weeks for some side effects (e.g., sedation, postural hypotension) to decrease if benefits are seen and side effects are not intolerable or dangerous.
- Consider changing antipsychotics if extrapyramidal side effects (EPS), akathisia, or other complaints such as dysphoria and zombie-like feelings develop, or if multiple medications for side effects are necessary.
- Use lowest dosing frequency (once daily or twice daily) and consider using pill boxes and techniques such as reminders to facilitate medication adherence.

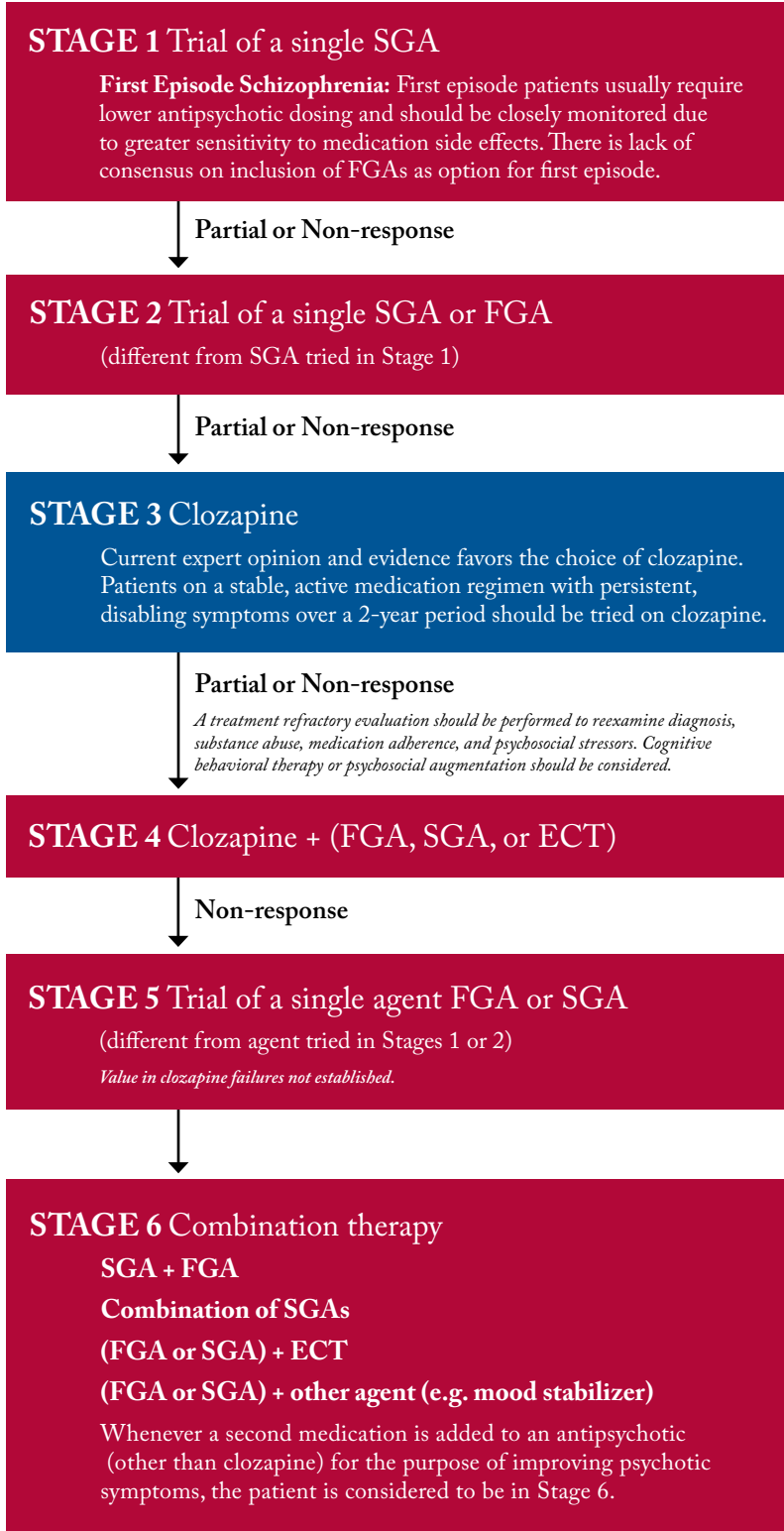
This information is intended to supplement the knowledge of clinicians regarding best practices and drug therapy to treat schizophrenia in non-pregnant individuals ages 18-64. It is advisory only and is not intended to replace, nor should it be regarded as, a substitute for individualized diagnosis and treatment, based upon sound clinical judgment. Evidence-based materials and algorithms developed and implemented in the Texas Medication Algorithm Project (TMAP) provide the primary source of information. Modifications were made (with permission) to the TMAP content and algorithms as necessary for the SCORxE project. See the accompanying evidence document for references and details of recommendations.

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Antipsychotic Algorithm

Choice of antipsychotic (AP) should be guided by considering the patient's clinical characteristics and the efficacy and side effect profiles of the medication. If patient is inadequately adherent at any stage, the clinician should assess and consider a long-acting antipsychotic preparation, such as risperidone long-acting injection, haloperidol decanoate, or fluphenazine decanoate.



Consider move to clozapine in patients with a history of suicidality (Level a), violence (Level b), or comorbid substance abuse (Level b/c).

Any stage(s) can be skipped depending on clinical picture or history of antipsychotic failure. Similarly, may go back to previous stage based upon past response.

CDPs for Stages 1, 2, 4, 5, and 6 generally occur at Weeks 0, 5, 8, and 12

- Titrate the new medication to therapeutic dose within one week.
- Go to maintenance if see response.
- Adjust dose or continue AP if partial response.
- Go to next stage if no response.

CDPs for Stage 3 generally occur at Weeks 0, 16, and 28

- Titrate clozapine to therapeutic dose (at least 300 mg/day) within one month.
- Go to maintenance if see response.
- Week 16: Get serum level and adjust dose if partial response or no response.
- Week 28: Further dose adjustments and/or add second AP or ECT if partial response. Add second AP or ECT if no response.

- KEY**
- FGA** First generation antipsychotic
 - SGA** Second generation antipsychotic
 - CDP** Critical Decision Point
 - AP** Antipsychotic medication
 - ECT** Electroconvulsive therapy

First Generation Antipsychotic (FGA) Dosage Guidelines

Drug	Starting Dose	Dose Range	Usual Maximum Dose
Chlorpromazine	50–100 mg/day	300–1,000 mg/day	1,000 mg/day
Fluphenazine	5 mg/day	5–20 mg/day	20 mg/day
Fluphenazine D*	12.5–25 mg IM every 2–3 weeks	6.25–50 mg IM every 2–4 weeks	100 mg IM every 4 weeks
Haloperidol	2–5 mg/day	2–20 mg/day	20 mg/day
Haloperidol D*	25–50 mg IM every 2 weeks	50–200 mg IM every 2–4 weeks	300 mg IM every 3–4 weeks
Loxapine	20 mg/day	50–150 mg/day	150 mg/day
Molindone	20 mg/day	50–150 mg/day	150 mg/day
Perphenazine	4–8 mg/day	16–64 mg/day	64 mg/day
Thiothixene	5–10 mg/day	15–50 mg/day	50 mg/day
Trifluoperazine	2 mg BID	5–40 mg/day	40 mg/day

*D: decanoate

Second Generation Antipsychotic (SGA) Dosage Guidelines

SGA	Starting Dose(i)	Titration	Range	Maximum Dose	Schedule
Aripiprazole	10 mg/day	5–10 mg every 10–14 days	15–30 mg/day	30 mg/day	AM or HS
Clozapine	12.5 mg HS (Half a 25 mg tab) Starting Day 3, dose increased every 3 days.	Day 2: 25 mg HS Day 3: 25 mg BID Day 6: 25 mg AM, 50 mg HS Day 9: 50 mg BID Day 12: 75 mg BID Day 15: 100 mg BID Day 18: 125 mg BID Day 21: 150 mg BID Day 24: 100 mg AM, 200 mg HS	300–900 mg/day (obtain serum level for doses > 600 mg/day)	900 mg/day	BID Eventual maintenance dose schedule is: BID (1/3 in am, 2/3 in pm). Some patients can be maintained on qHS dosing.
Olanzapine	5–10 mg/day	5 mg every 3–7 days	10–20 mg/day	40 mg/day (ii)	HS
Paliperidone	3 mg/day	3 mg every day	6–12 mg/day	12 mg/day	HS or AM
Quetiapine	100–200 mg/day	50–100 mg every 2–3 days	300–800 mg/day	800 mg/day (iii)	HS or BID
Risperidone	1–2 mg/day	1–2 mg every 2–3 days	2–6 mg/day	16 mg/day (iv)	HS or AM
Risperidone Long-acting Injection	If oral dose ≤ 2 mg, 25 mg IM If oral dose 3–4 mg, 37.5 mg IM If oral dose 5–6 mg, 50 mg IM	25 mg every 4 weeks	25–50 mg every 2 weeks	50 mg every 2 weeks	Every 2 weeks
Ziprasidone	80–120 mg/day	40 mg every 2–3 days	80–240 mg/day (v) (vi)	240 mg/day (v) (vi)	AM or BID The presence of food can increase ziprasidone's absorption up to 2-fold.

(i) Starting doses for individual patients may need to be lower. (ii) Manufacturer maximum recommended dose is 20 mg/day. Some data indicate that olanzapine doses > 20 mg may benefit patients who only partially respond to an adequate trial of olanzapine 20 mg. (iii) Higher doses are used clinically and may provide additional response per the SCORxE Mental Health Panel. (iv) The risk of extrapyramidal side effects is significantly increased by using doses > 6 mg daily. (v) SCORxE Mental Health Panel consensus (vi) Manufacturer maximum recommended dose is 160 mg/day.

Comparison of Side Effects of the Different Agents

Antipsychotic	Extrapyramidal Side Effects	Tardive Dyskinesia	Orthostatic Hypotension	Prolactin	Sedation	Weight Gain	Anticholinergic Side Effects	Dyslipidemia	Glucose Dysregulation
Chlorpromazine	++	+++	++++	++	++++	++	+++	-	-
Haloperidol	++++	++++	+	+++	+	+	+	-	-
Aripiprazole	+/-	+/-	-	-	+	+/-	+	+/-	+
Clozapine	+/-	-	+++	+/-	++++	++++	++++	++++	+++
Olanzapine	+	+	+	+/-	+++	+++	++	++++	+++
Paliperidone (i)	+ / ++	+	+	+++	+	++	+	+	+
Quetiapine	+/-	+/-	++	+/-	++++ (ii)	++	+	+	+
Risperidone	+ / ++ (iii)	+	+	+++	+	++	+	+	+
Ziprasidone	+	+	+	+	+	+/-	+	+/-	-

- none +/- mild to none + mild ++ moderate +++ moderately severe ++++ severe

(i) Paliperidone adverse effects based on available data and risperidone data (ii) During dose titration phase (iii) ++ at doses > 6 mg/day

Score Sheet: 4-Item Positive Symptom Rating Scale and Brief Negative Symptom Assessment

4-Item Positive Symptom Rating Scale* NA=not able to be assessed 1=symptom not present 6/7=severe/extremely severe

1. Suspiciousness	NA	1	2	3	4	5	6	7	
2. Unusual Thought Content	NA	1	2	3	4	5	6	7	
3. Hallucinations	NA	1	2	3	4	5	6	7	
4. Conceptual Disorganization	NA	1	2	3	4	5	6	7	SCORE: _____

*A response is considered a 20% reduction in symptoms from initiation of treatment.

4-Item Negative Symptom Rating Scale 1=symptom not present 6=severe

1. Prolonged Time to Respond	1	2	3	4	5	6	
2. Emotion. (Unchanging facial expression; blank, expressionless face)	1	2	3	4	5	6	
3. Reduced Social Drive	1	2	3	4	5	6	
4. Poor Grooming and Hygiene	1	2	3	4	5	6	SCORE: _____

Source of Information (check all applicable):

- Patient
- Parents/Relatives
- Mental Health Professionals
- Chart

Explain here if validity of assessment is questionable:

- Symptoms possibly drug-induced
- Underreported due to lack of rapport
- Underreported due to negative symptoms
- Patient uncooperative
- Difficult to assess due to formal thought disorder
- Other _____

Confidence in Assessment (scale of 0 to 5)

1=not at all 5=very confident

SCORE: _____

Patient Global Self Report (scale of 0 to 10)

0=no symptoms/side effects 5=moderate 10=very severe

Symptoms SCORE: _____ Side Effects SCORE: _____

The 4-Item Positive Symptom Rating Scale was adapted from the Expanded Version of the BPRS developed by: Ventura J, Lukoff D, Nuechterlein KH, Liberman RP, Green MF, and Shaner. A Manual for the expanded Brief Psychiatric Rating Scale. *International Journal of Methods Psychiatry Research*, 3:227-244, 1993.

The Brief Negative Symptom Assessment was adapted from the Negative Symptom Assessment and the Scale for the Assessment of Negative Symptoms developed respectively by: Alphas and Summerfelt. *The Negative Symptom Assessment: A new instrument to assess negative symptoms of schizophrenia*. Psychopharmacology Bulletin, 1989. 25 (2): p. 159-163 and Andreason, N. *Modified scale for the assessment of negative symptoms. NIMH treatment strategies in schizophrenia study*. Public Health Administration. U.S. Department of Health and Human Services, 1984. ADM (9/85): p. 9-102.