MANAGEMENT OF SCHIZOPHRENIA IN ADULTS

QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MINISTRY OF HEALTH MALAYSIA
MALAYSIAN PSYCHIATRIC ASSOCIATION
ACADEMY OF MEDICINE MALAYSIA
KEY MESSAGES

- Schizophrenia is a major psychiatric disorder that alters an individual's perception, thought, affect and behaviour.
- The incidence rate is 16 per 100,000 (range of 8 to 43 per 100,000).
- Although there is effective biopsychosocial treatment available, substantial number of people with schizophrenia remains undiagnosed and untreated.
- People who develop symptoms of schizophrenia should be diagnosed and treated early.
- The management of schizophrenia may be divided into acute phase, relapse prevention and stable phase.
- Antipsychotics (APs) are the mainstay of pharmacological treatment. Conventional APs should be used as a first option; most commonly used are haloperidol, perphenazine or sulpiride. As options, amisulpride or olanzapine may also be considered.
- Effective psychosocial interventions include family intervention, psychoeducation, social skills training and cognitive remediation therapy.
- It is essential that the following services be considered i.e. community mental health team to prevent relapse and readmission, assertive community treatment for more difficult cases, supported employment for all who want to work, and crisis intervention and home treatment as alternative to acute inpatient care.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Schizophrenia in Adults (May 2009).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

- Ministry of Health Malaysia : http://www.moh.gov.my
- Academy of Medicine Malaysia : http://www.acadmed.org.my
- Malaysian Psychiatric Association : http://www.psychiatry-malaysia.org
DIAGNOSTIC CRITERIA

International Classification of Diseases-10 (ICD-10)

F20  Schizophrenia:

Characterised by:
- distortions of thinking and perception
- inappropriate or blunted affects
- clear consciousness and intellectual capacity maintained
- certain cognitive deficits may evolve over time
- the most important psychopathological phenomena include
  - thought echo
  - thought insertion or withdrawal
  - thought broadcasting
  - delusional perception and delusion of control
  - influence of passivity
  - third person hallucination
  - negative symptoms

The course of schizophrenic disorders can be either continuous, or episodic with progressive or stable deficit, or there can be one or more episodes with complete or incomplete remission.

The following should be excluded:
- bipolar disorder
- overt brain disease
- drug intoxication or withdrawal

CRITERIA FOR EARLY REFERRAL TO SPECIALIST CARE

- Prodromal or attenuated symptoms
- Unclear diagnosis
- Treatment adherence issues
- Poor response to treatment
- Potential violent behaviour to self or others
- Drug-related complications
- Plan for psychosocial rehabilitation
- Co-morbid substance abuse
- Special group e.g. pregnancy, paediatric and geriatric age

CRITERIA FOR HOSPITALISATION

- Risk of harm/neglect to self or others
- Deterioration in psychosocial functioning
- Serious/life-threatening drug reactions
ALGORITHM FOR MANAGEMENT OF SCHIZOPHRENIA

**Diagnosis of schizophrenia**

**Identify phases of illness**

**Acute phase**

Need rapid tranquilisation

- **YES**
  - Urgent
    - **YES**
      - Combination of parenteral treatment
    - **NO**
      - Oral medication is preferred
      - When parenteral needed, use a single agent

- **NO**
  - Provide comprehensive plan (pharmacological, psychosocial & service level interventions)
  - Offer conventional APs (300-1000mg CPZ equivalent) or AMS or OLZ
  - Monitor clinical response, side effects & treatment adherence

**Poor response**

- **YES**
  - Adequate dose & duration
    - **YES**
      - Exclude substance abuse, treatment non-adherence & concurrent other general medical conditions
      - Optimise psychosocial interventions
      - Refer to psychiatrist for trial of clozapine
    - **NO**
      - Optimise APs usage

- **NO**
  - Relapse prevention
    - Plan for recovery (ACT, family intervention, psychoeducation, social skills training & supported employment)
    - APs usage to continue with single oral agent from acute phase; use depot when non-adherent
    - Monitor for clinical response, side effects & treatment adherence

**Stable phase**

- Follow-up at primary care
- Follow manual on Garispanduan Perkhidmatan Rawatan Susutan Pesakit Mental di Klinik Kesihatan

- Prevention & management of side effects of APs at all phases
  - Monitor EPS/akathisia/weight gain/diabetes/heart disease/sexual dysfunction
  - Follow schedule of physical care as per follow-up manual
**Diagnosis of schizophrenia**

- **Monotherapy with AP except clozapine for 6 – 8 weeks**
  - IR/ISE*

- **Monotherapy with different AP except clozapine for 6 – 8 weeks**
  - IR/ISE

- **Clozapine**
  - IR/ISE

- **Clozapine + AP or ECT**
  - IR/ISE

- **Combination therapy e.g. combination of APs, APs + ECT, or APs + mood stabiliser**

**Good clinical response**

**Relapse prevention** (refer algorithm on Management of Schizophrenia)

- Consider earlier trial of clozapine in:
  - recurrent suicidal idea
  - recurrent aggressive behaviour
  - co-morbid substance abuse
  - persistent positive symptoms > 2 years

**When rapid tranquillisation needed:**

- use oral lorazepam or diazepam or haloperidol or risperidone
- if parenteral needed, use single agent IM haloperidol or IM lorazepam or IV diazepam
- if urgent, use combination of IM haloperidol + either IM lorazepam or IV diazepam or IM promethazine

* IR/ISE = Insufficient response/intolerable side effects
** Refer to psychiatrist for trial of clozapine
<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Target Dose or Range</th>
<th>Antipsychotic Schedule</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amisulpride (Solian)</td>
<td>50 mg/day</td>
<td>50-300 mg for negative symptoms 400-800 mg for positive symptoms</td>
<td>Once daily If more than 400 mg, twice daily</td>
<td>Insomnia Anxiety Agitation Somnolence Nausea Dry mouth Acute dystonia Galactorrhoea</td>
</tr>
<tr>
<td>Aripiprazole (Abilify)</td>
<td>10-15 mg/day</td>
<td>10-30 mg/day</td>
<td>Once daily</td>
<td>Agitation Constipation EPS Insomnia Nausea Somnolence</td>
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<tr>
<td>Generic available</td>
<td></td>
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<tr>
<td>Olanzapine (Zyprexa)</td>
<td>5-10 mg/day</td>
<td>10-20 mg/day</td>
<td>Once daily</td>
<td>Constipation Dizziness Dry mouth IGT Hyperlipidaemia Increased appetite Sedation Weight gain</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>50 mg/day</td>
<td>300-800 mg/day</td>
<td>Twice daily</td>
<td>Dry mouth IGT Headache Hyperlipidaemia Increased appetite Orthostatic hypotension Sedation Weight gain</td>
</tr>
<tr>
<td>Paliperidone (Invega)</td>
<td>3 mg/day</td>
<td>6-12 mg/day</td>
<td>Once in the morning</td>
<td>EPS IGT Galactorrhoea Hyperlipidaemia Menstrual irregularity Orthostatic hypotension Prolactin elevation Sedation Sexual dysfunction Tardive dyskinesia Weight gain</td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>1-2 mg/day</td>
<td>2-6 mg/day</td>
<td>Once daily</td>
<td>Galactorrhoea Hyperlipidaemia Menstrual irregularity Orthostatic hypotension Prolactin elevation Sedation Sexual dysfunction Tardive dyskinesia Weight gain</td>
</tr>
<tr>
<td>Generic available</td>
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<tr>
<td>Risperidone microspheres long-acting injection (Consta)</td>
<td>25 mg/2 weeks</td>
<td>25-50 mg/2 weeks</td>
<td>Once every 2 weeks</td>
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<tr>
<td>Drug</td>
<td>Starting Dose</td>
<td>Target Dose or Range</td>
<td>Antipsychotic Schedule</td>
<td>Side Effects</td>
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<tr>
<td>Clozapine (Clozaril)</td>
<td>12.5 mg/day</td>
<td>300-900 mg/day (serum level for doses &gt; 600 mg/day)</td>
<td>Twice daily</td>
<td>Agranulocytosis Excess salivation Fever IGT Hyperlipidaemia Increased appetite Myocarditis Orthostatic hypotension Sedation Seizures Tachycardia Weight gain</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>50-100 mg/day</td>
<td>300-1000 mg/day</td>
<td>3 times daily</td>
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<tr>
<td>Perphenazine</td>
<td>4-8 mg/day</td>
<td>16-64 mg/day</td>
<td>3 times daily</td>
<td>constipation Dry mouth EPS Orthostatic hypotension Photosensitivity Sedation Tachycardia Tardive dyskinesia</td>
</tr>
<tr>
<td>Fluphenazine depot (Mocacte)</td>
<td>12.5-25 mg IM/1-3 weeks</td>
<td>6.25-50 mg IM/2-4 weeks</td>
<td>Every 1-3 weeks</td>
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<tr>
<td>Flupenthixol decanoate (Fluanxol)</td>
<td>10-20 mg IM/ 1-3 weeks</td>
<td>10-40 mg IM/2-4 weeks</td>
<td>Every 1-3 weeks</td>
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<tr>
<td>Haloperidol</td>
<td>2-5 mg/day</td>
<td>2-20 mg/day</td>
<td>1-3 times daily</td>
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<tr>
<td>Sulpiride (Generic available)</td>
<td>200-400 mg/ day</td>
<td>400-800 mg/day</td>
<td>Twice daily</td>
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<tr>
<td>Zuclopenthixol acetate (Acuphase)</td>
<td>50-100 mg IM/ 2-3 days</td>
<td>50-200 mg/ 3 days</td>
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</tr>
<tr>
<td>Zuclopenthixol decanoate (Clopixol depot)</td>
<td>100-200 mg IM/ 1-3 weeks</td>
<td>100-400 mg/ 1-3 weeks</td>
<td>Every 1-3 weeks</td>
<td></td>
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</tbody>
</table>
## PATIENT MONITORING PARAMETERS

<table>
<thead>
<tr>
<th>Test</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>At every visit</td>
</tr>
<tr>
<td>Blood pressure and pulse rate</td>
<td>At every visit</td>
</tr>
<tr>
<td>Side effects</td>
<td>At every visit (follow Senarai Semak Kesan Sampingan Ubat-ubatan Psikotopik/PKM 17/2001 PIN 2003)</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>At least once for patient &gt; 40 years old or as clinically indicated</td>
</tr>
<tr>
<td>Total White Blood Count</td>
<td>a. upon starting AP</td>
</tr>
<tr>
<td></td>
<td>b. for clozapine:</td>
</tr>
<tr>
<td></td>
<td>• every week for first 18 weeks</td>
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<tr>
<td></td>
<td>• every month after that for first year</td>
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<tr>
<td></td>
<td>• every visit subsequently</td>
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<tr>
<td>Fasting plasma glucose level + haemoglobin A1c</td>
<td>a. upon starting AP treatment and yearly</td>
</tr>
<tr>
<td></td>
<td>b. if patient has risk factor for Diabetes Mellitus</td>
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<tr>
<td></td>
<td>• upon starting</td>
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<tr>
<td></td>
<td>• at four months</td>
</tr>
<tr>
<td></td>
<td>• every year subsequently</td>
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<tr>
<td>Lipid screening</td>
<td>Upon starting and</td>
</tr>
<tr>
<td></td>
<td>• every two years if lipid levels are normal</td>
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<tr>
<td></td>
<td>• every 6 months if Low Density Lipoprotein (LDL) level is &gt; 3.3.mmol/L</td>
</tr>
<tr>
<td>Pregnancy test</td>
<td>As clinically indicated</td>
</tr>
</tbody>
</table>