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Canadian Consortium for Early Intervention in Psychosis

PATIENT INFORMATION

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Cannabis and Early Psychosis Order Set	ACTION

Administration

Document Purpose

This order set may be used to help guide the evaluation and treatment of patients with early psychosis associated with cannabis use in both the inpatient and outpatient care setting.

Working Diagnoses

Diagnosis based on criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)[1]

Psychotic Disorder Diagnosis

☐ Cannabis-induced Psychotic Disorder
☐ Brief Psychotic Disorder
☐ Bipolar I Disorder with Psychotic Features
☐ Major Depressive Disorder with Psychotic Features
☐ Schizophrenia
☐ Schizoaffective Disorder
☐ Schizophreniform Disorder
☐ Psychotic Disorder Not Otherwise Specified
☐ Other (specify): ____________________

Substance Use Disorder Diagnosis

☐ Comorbid Cannabis Use Disorder (CUD) - Severity: ☐ Mild ☐ Moderate ☐ Severe
☐ Other Comorbid Substance Use Disorder (SUD) (e.g. cocaine, methamphetamine, opioid): ____________________
____

Comorbid Diagnosis

Comorbid Diagnoses (psychiatric and relevant comorbid medical condition)

☐ ____________________

Risk Assessment

☒ Assess for suicide risk[2–4]:
- ☐ Clinical interview
- ☐ Validated screening tool (e.g. Beck Scale for Suicidal Ideation [BSSI], Columbia-Suicide Severity Rating Scale [C-SSRS])[4]: ____________________

☒ Assess for risk of violence[2,5]:
- ☐ Clinical interview
- ☐ Validated screening tool (e.g. Dynamic Appraisal of Situational Aggression: Inpatient Version [DASA-IV][6], Short-Term Assessment of Risk and Treatability [START]): ____________________

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Cannabis Use History

☒ Screen for cannabis use:

☐ Clinical interview, including information about[2,7]:

- Cannabis products used (e.g. combustibles, edibles, oils)
- Cannabinoid content (e.g. percentage of THC, CBD)
- Age of onset of regular cannabis use
- Frequency, quantity, route of administration and pattern of cannabis use
- Source of cannabis (i.e. how is it obtained)
- Risky cannabis use (e.g. use before driving, use at school/work, use with other substances)
- Motivation for use (e.g. pleasure/recreation, peer-pressure, coping)

☐ Structured Clinical Interview for DSM-5 (SCID-5) for CUD

☐ Validated screening tool[8–11]:

☐ Timeline Follow Back (TLFB)
☐ Problematic use of Marijuana (PUM)
☐ Severity of Dependence Scale (SDS)
☐ Cannabis Abuse Screening Test (CAST)
☐ Cannabis Use Disorder Identification Test – Revised (CUDIT-R)
☐ Other (specify): ________________________________

Other Screening

Other Substance Use Screening

Diagnosis and severity of substance use disorder should be made based on DSM-5 criteria with severity assessment

☒ Screen for other substance use[2,7]:

☐ Clinical interview

☐ Validated screening tool (e.g. Alcohol Use Disorders Identification Test [AUDIT], Drug Abuse Screening Test [DAST-10), NIDA-Modified ASSIST[12]): ________________________________

Tobacco and Nicotine Status Screening

☒ Screen for tobacco/nicotine use status (e.g. smoking, vaping, chewing):[7,13]

☐ Clinical interview

☐ Validated screening tool (e.g. Fagerstrom Test for Nicotine Dependence[14]): ________________

Further Assessments

Lab Investigations

Hepatitis serology, HIV testing and syphilis serology should be considered if risk factors are present

☐ Urine drug screen[15]
☐ Urine β-HCG
☐ Other (specify): ________________

Diagnostics

Routine neuroimaging is not recommended in FEP in the absence of neurologic signs and symptoms*[2,16,17]

An ECG should be considered for the patient with severe cannabis intoxication[5,7]

☐ ECG[5,18] Reason: ________________________________

☐ ____________ Reason: ________________________________

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Psychiatric Symptoms Assessment Tools

☒ Clinical Global Impression-Severity (CGI-S) Scale[19]:

Considering your total clinical experience with this population, how mentally ill is the patient. Select one:

☐ 1 = Normal ☐ 2 = Borderline mentally ill ☐ 3 = Mildly ill ☐ 4 = Moderately ill

☐ 5 = Markedly ill ☐ 6 = Severely ill ☐ 7 = Among the most extremely ill patients

☐ Brief Psychiatric Rating Scale (BPRS) 4-Item Positive Symptom Rating Scale available at:
http://academicdepartments.musc.edu/cop/research/SCORxE%20pdfs/padforproofing%20accessible.pdf

☐ Other (specify): ______________________________

Assessment of Capacity to Consent

☐ Capable

☐ Incapable, as per local capacity definition/requirements

☐ Further treatment capacity assessment required

Management of Psychosis

Refer to Antipsychotic Treatment Selection Tool available at: https://vivomap.ca/lib/surveyStandalone/psychosis.php

Refer to the OPTIMA Tool, available at: http://epicanada.org/news/optima-offering-patients-therapeutic-information-on-medication-alternatives/

Antipsychotic medication remains the mainstay of treatment for persons with psychotic disorders, whether or not they have a coexisting substance use disorder7

Patients should be treated as they would a first-episode psychosis with a minimum treatment duration of 18-months unless there is rapid resolution of psychotic symptoms with full remission and recovery[7]

Atypical Antipsychotics

Oral Medication with LAI Formulations

☐ aripiprazole ___________ mg PO q24h (10 – 30 mg)

☐ paliperidone ___________ mg PO q24h (3 – 12 mg)

☐ risperidone ___________ mg PO q24h (2 – 8 mg)

LAI Formulation Antipsychotic Medication

Tolerability with equivalent oral antipsychotic should be established prior to initiating treatment with LAI formulation[20]

LAI formulations may prevent relapses and rehospitalizations if adherence is further complicated by SUD[21]

LAI Aripiprazole Initiation

☐ aripiprazole monohydrate ___________ mg IM q28days (300 – 400 mg) start on ___________ (yyyy-mm-dd)

And ☐ aripiprazole monohydrate _________ mg PO q24h (10 – 30 mg) for 14 days

LAI Paliperidone Initiation

☐ paliperidone palmitate ___________ mg IM for one dose (100 – 150 mg) on __________ (yyyy-mm-dd) (Day 1)

Then ☐ paliperidone palmitate ___________ mg IM for one dose (75 – 100 mg)
on ____________ (yyyy-mm-dd) (Day 8)

Then ☐ paliperidone palmitate ___________ mg IM q ________ days (25 – 150 mg, q28days)

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Management of Psychosis Continued…

Atypical Antipsychotics Continued…

LAI Risperidone Initiation

☐ risperidone__________ mg IM q2weeks (12.5 – 50 mg) start on __________ (yyyy-mm-dd)

And ☐ risperidone __________ mg PO q24h (2 – 8 mg) for 3 weeks

Oral Medication Initiation without LAI Formulation

☐ asenapine ____________ mg Sublingual q12h (5 mg; assess tolerability for 1 week before titrating)
☐ brexpiprazole __________ mg PO q24h (1 mg; assess tolerability for 4 days before titrating)
☐ lurasidone ____________ mg PO q24h with food (40 mg; assess tolerability over several days before titrating)
☐ olanzapine ____________ mg PO q24h (5 – 10 mg)
☐ quetiapine ____________ mg PO q __________ h (25 – 400 mg, q12h)
☐ ziprasidone ___________ mg PO q12h with food (20 mg; assess tolerability for 2 days before titrating)
☐ ____

Initiation of Clozapine

Clozapine should be considered for patients who have failed to respond to two previous adequate trials of antipsychotic medications[22,23]

☐ Initiate clozapine pretreatment assessment and refer to your site's clozapine initiation order set or protocol

Alternate Antipsychotics

☐ ____

Management of Agitation

The most severe effects of cannabis intoxication are best treated symptomatically with a benzodiazepine or atypical antipsychotic medication. No medication is approved specifically for treatment of cannabis intoxication[24]

Benzodiazepines

Concomitant use of benzodiazepines and antipsychotics may produce marked CNS depressant effects[25]

☐ lorazepam _________ mg Sublingual q _______ h PRN for acute agitation (1 – 2 mg)[26]; **max** ________ **in 24 hours**
☐ lorazepam _________ mg IM q ________ h PRN for acute agitation (0.5 – 2 mg)[26]; **max** ____________ **in 24 hours**
☐ ____

Antipsychotics

If antipsychotic already ordered for management of psychosis, prescriber to assess if additional medication required

☐ aripiprazole[27] __________ mg PO q _______ h PRN for acute agitation (10 – 15 mg); **max** __________ **in 24 hours**
☐ olanzapine _________ mg PO q ________ h PRN for acute agitation (2.5 – 10 mg)[26]; **max** ___________ **in 24 hours**
☐ olanzapine _________ mg IM q ________ h PRN for acute agitation (2.5 – 10 mg)[26]; **max** ___________ **in 24 hours**
☐ risperidone[27] _____________ mg PO q __________ h PRN for acute agitation (1 – 2 mg); **max** _______ **in 24 hours**
☐ haloperidol[27] __________ mg PO q _______ h PRN for acute agitation (0.5 – 10 mg); **max** __________ **in 24 hours**
☐ haloperidol[27] __________ mg IM q _____ h PRN for acute agitation (2 – 10 mg); **max** ______________ **in 24 hours**
☐ ____

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Therapy

The best intervention for reducing the frequency and severity of cannabis use focusses on psychosocial interventions. Evidence shows that cognitive behavioural therapy (CBT), motivational interviewing (MI), brief interventions (BI) and contingency management (CM) have the potential to be effective[28]

Stage of Change for Cannabis Use[7,29]

Please indicate patient's current stage of change regarding cannabis use:

- ☐ Pre-contemplative (not currently open to changing cannabis use)
- ☐ Contemplative (considering changing cannabis use)
- ☐ Preparatory (open to change and planning to change cannabis use)
- ☐ Action (currently changing cannabis use and habits)
- ☐ Maintenance (cannabis use has stopped)

Motivational Interviewing (MI)[28]

☐ Assess/screen for appropriateness for MI cannabis use disorder[28]

Refer for MI: ☐ Yes ☐ No ☐ Further assessment required

☐ If MI appropriate for patient and not referred, please provide explanation (e.g. services not available):

____

Cognitive Behavioural Therapy (CBT)

☐ Assess/screen for appropriateness for CBT for psychosis and/or cannabis use disorder[22,28,30]

Refer for CBT[18,28]: ☐ Yes ☐ No ☐ Further assessment required

☐ If CBT appropriate for patient and not referred, please provide explanation (e.g. services not available):

____

Referrals

Long-term therapy may be necessary for patients with severe CUD with acute psychosis who refuse hospitalisation

Integration of intervention for addiction within the FEP setting presents advantages and a more structured care plan

- ☐ Addiction Services
- ☐ Addiction Day Treatment
- ☐ Concurrent Disorders Programming
- ☐ Family Therapy[18,30]
- ☐ Outpatient Addiction Counselling:
  - ☐ Integrated with Case Management
  - ☐ Within First Episode Psychosis (FEP) Clinic
  - ☐ Other - Reason: ______________________________
- ☐ Peer Support
- ☐ Residential Addiction Treatment
- ☐ Social Work
- ☐ Other (supported employment program, cognitive remediation therapy [CRT], social skills training, life skills training)[30]: __

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Psychoeducation and Health Lifestyle Information

☐ Provide education to patient on the following topics verbally, in writing, and electronically, as applicable[18]:

- Diagnosis and course of psychosis and SUD/prognosis/recovery
- Impact of cannabis and substance use on psychosis, relevance of abstinence from cannabis or reduction and relapse prevention[31]
- The components of cannabis (i.e. cannabidiol [CBD], tetrahydrocannabinol [THC]) and potencies
- Pharmacological treatment options for psychosis and SUD, including their potential efficacy and side effects
- Alternate treatment options
- Psychosocial treatment options for psychosis and SUD
- Risk of relapse of psychosis and recognition of warning signs and psychosis relapse prevention strategies
- Risk of suicide and monitoring for warning signs
- Risk of violent behavior and monitoring of warning signs
- Importance of adherence with treatment and follow-up as well as adherence enhancement strategies

☐ Provide the following resources to patient regarding cannabis use:

- Low-risk Cannabis Use Guidelines (LRCUG) - https://www.camh.ca/-/media/files/pdfs---reports-and-books---research/canadas-lower-risk-guidelines-cannabis-pdf.pdf
- CCEIP Cannabis Use Tear Pad - http://mycannabisiq.ca/wp-content/uploads/2018/07/2018-CCEIP-Cannabis-Tear-Pad-EN-pdf.pdf
- Government of Canada: Cannabis - https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis.html

☐ Offer family therapy and provide family-focused psychoeducation and support[18,22,28,30]

☐ Provide education on healthy eating, physical activity[13,18]

☐ Provide patient and family with contact information for local crisis supports,[18] SUD treatment centers, inpatient treatment centers, outpatient treatment resources, and integrated treatment supports (specify): ______________________________

Additional Orders

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Order Set Development and Implementation Considerations

Abbreviations

Cannabidiol = CBD
First Episode Psychosis = FEP
Tetrahydrocannabinol = THC
Cannabis Use Disorder = CUD
Substance Use Disorder = SUD

The recommendations in this document are intended as general guidance, and do not replace clinical judgement. Physicians must consider relative risks and benefits in each patient when applying these recommendations

- **Cannabis Use Disorder (CUD) Diagnostic Criteria**: As defined by the DSM 5th Edition:
  - A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
    - Cannabis is often taken in larger amounts or over a longer period than was intended
    - There is a persistent desire or unsuccessful efforts to cut down or control cannabis use
    - A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects
    - Craving, or a strong desire or urge to use cannabis
    - Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school or home
    - Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis
    - Important social, occupational, or recreational activities are given up or reduced because of cannabis use
    - Recurrent cannabis use in situations in which it is physically hazardous
    - Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis
    - Tolerance, as defined by either of the following:
      - A need for markedly increased amounts of cannabis to achieve intoxication or desired effect
      - Markedly diminished effect with continued use of the same amount of cannabis
    - Withdrawal, as manifested by either of the following:
      - The characteristic withdrawal syndrome for cannabis
      - Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal syndrome[38]
- **Cannabis Drug Testing**[33]: Urine drug testing for cannabis is based on THC's main metabolite (11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid). Estimating the detection time for cannabis in urine is complicated as there are many factors that impact this result, such as: route of administration, dosage, potency, frequency of use, body mass, and metabolic rate. As cannabinoids are highly lipophilic, chronic users will accumulate THC in fatty tissues, which results in a slower elimination of cannabis out of the body. This helps explain why detection of cannabis can occur in the urine for more than 30 days after cessation among chronic users, whereas a single-use case may have levels detected for only up to 72 hours. However, it is difficult to differentiate an acute versus chronic cannabis user from urine drug tests and quantifying conjugates of THC as biomarkers has not proved reliable. Blood tests may be unreliable as blood concentrations of cannabis can decrease quickly in the first hour after exposure due to the distribution of cannabis into fat stores. It is there important to perform a thorough assessment on patients with a history of cannabis use.
- **Cannabis Use and Psychosis**: Studies have demonstrated that cannabis use is an independent risk factor in the development of psychotic disorders, especially among those with a genetic predisposition for developing schizophrenia and those who have previously experienced psychotic symptoms.[7] Substance use increases the risk of developing psychotic symptoms and also worsens the outcomes in those with schizophrenia and other types of psychosis (e.g. more positive symptoms, higher rates of nonadherence, greater relapse rates, depression, lower functioning, etc.).[7] Some

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studies show that more than 50% of patients presenting with FEP consumed cannabis regularly, and 44% of individuals with FEP having CUD.[21]

- **Cannabis Use and Schizophrenia**[3]: Studies have shown that cannabis use and cannabis-induced psychosis increase the risk of schizophrenia and is associated with an earlier onset of schizophrenia. Cannabis-induced psychosis diagnosis converts to schizophrenia in up to 50% of cases and to other severe mental illnesses in another 25% of cases. The age group with the highest risk of converting to schizophrenia were those between 16 to 25 years of age. Patients with a past psychiatric history (e.g. pre-existing substance use disorder, personality disorder) have a higher risk of converting to schizophrenia than those who do not. Overall, patients with a cannabis-induced psychosis should be offered follow-up for potential early identification and management of schizophrenia or other mental health disorders.
- **Cannabidiol (CBD)**: There are some studies that propose that CBD could mitigate the temporary symptoms of psychosis that are exacerbated by THC and that CBD could be potentially beneficial used as an adjunct to antipsychotic therapy in those with schizophrenia to reduce psychotic symptoms.[35,36] More research needs to be done in this area and no recommendations can be made at this time.
- **Tetrahydrocannabinol (THC)**[35]: The association between cannabis use and psychosis is believed to be primarily related to THC as THC is the main psychoactive component in cannabis that interacts with the dopamine system and causes increases in dopamine release and nerve activity. It is believed that higher THC concentrations are associated with a higher risk of psychosis.
- **Brief Intervention (BI)**: BIs aim to identify current problems among those with substance use and motivate those at risk to change their substance use behaviours and habits.[29] A BI can range from 5 of brief advice to 30 minutes brief counselling.[29] BIs are not intended to treat people with serious substance dependence but rather offer valuable tools for treatment of problematic or risk substance use.[29] The FRAMES model helps describe the main principles underlying BIs:
  - **Feedback**: Provide feedback to patient on the risks and negative consequences of substance use; observe the patient's reaction
  - **Responsibility**: Explain to the patient that he or she is responsible for making his or her own decision about substance use
  - **Advice**: Provide clear and practical advice on modifying substance use
  - **Menu of alternative change options**: Provide the patient with a variety of change options to choose from; empowering him or her to be involved in decision making
  - **Empathy**: Be empathetic, respectful and non-judgemental towards to patient
  - **Self efficacy (i.e. confidence)**: Encourage the patient to understand that he or she has the power to modify his or her substance use if he or she chooses
- **Contingency Management (CM)**[32]: CM is used in substance-use disorder management as a type of behavioural therapy designed to systematically arrange consequences, weaken drug use and strengthen abstinence. The main elements of CM are behavioural reinforcers and monitoring. CM focusses on operant conditioning, which assumes that a person is inclined to pursue behaviours that warrant positive consequences and discourages behaviours that produce negative consequences.
- **Clozapine and Substance Use Disorder**: Patients with schizophrenia and concurrent substance use disorder may benefit from clozapine therapy, which has been associated with a reduced rate of substance abuse relapses compared with other antipsychotics.[34]
- **Diagnostic Imaging**: Evidence suggests that routine neuroimaging in first episode psychoses does not yield findings which alter clinical management in a meaningful way.[16] Consider selective use of neuroimaging to exclude organic

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causes of psychosis where patient's symptoms, or other aspects of their presentation, suggest a higher likelihood of an underlying organic cause.[17]

- **Choice of Antipsychotics**: This order set reflects the general preference toward initiation of atypical antipsychotics prior to typical antipsychotics, according to review of current treatment guidelines[15,37] and expert consensus.
- **Antipsychotic Adequate Trial Duration**: This order set includes a definition for duration of adequate trial of antipsychotic medication, according to review of current treatment guidelines[15,23] and expert consensus.
- **Discharge Planning from Inpatient Admission**: Arrange for community follow-up appointment within 7 days of discharge from inpatient setting.[22] When discharging patient from inpatient setting, send the patient's care plan to their community team/provider who is accountable for coordinating, communicating and providing their care.[22]

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All medications have been reviewed using Lexicomp and Compendium of Pharmaceuticals and Specialties (eCPS).

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