Series in Professional Ethics

Prescriptions of Hypnotics, Benzodiazepines and Codeine Containing Cough Mixtures - Clinical Guidance and What You Need to Know About MOH Rules

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The improper prescribing of benzodiazepines (BZDs), hypnotics and codeine containing cough mixtures (CCCMs) all carry risk of misuse, abuse and dependence. All doctors are advised to familiarise themselves with the guidelines below and to comply with the requirements.

Benzodiazepines and Hypnotics

This section on BZDs and hypnotics takes reference from the following documents:

- The 2008 Ministry of Health (MOH) clinical practice guidelines (CPG) on the prescribing of benzodiazepines.[1]

- The 2008 administrative guidelines on the prescribing of benzodiazepines and other hypnotics.[2]

Definitions

Benzodiazepines (BZDs) are a class of drugs that have hypnotic, anxiolytic, muscle relaxant and anti-convulsant properties. Zopiclone (Imovane®) and Zolpidem (Stilnox®) are considered non-benzodiazepine hypnotics (non-BZDs). In this article the non-BZDs are referred to as hypnotics.

The BZDs and non-BZD's have similar profiles with respect to side-effects, dependence and tolerance. Therefore, the prescription of Zolpidem and Zopiclone should be treated with the same cautions as BZDs.

Indications For Use

There is a need for every doctor to ensure that BZDs/hypnotics are used appropriately to treat insomnia, anxiety and other psychiatric and medical conditions. Their inappropriate use can lead to undesired results or tolerance and drug dependence.

- A short course of 2 to 4 weeks of a BZD/hypnotic may be considered in acute insomnia (less than 4 weeks) if it is severe, distressing and disabling. It should be prescribed for intermittent use and only when necessary.

- For chronic insomnia (> 4 weeks), non-pharmacological therapies are the mainstays of management and BZD/hypnotic drug use should be avoided as far as possible. Doctors should routinely warn patients about rebound insomnia with the use of BZDs/hypnotics and document such warnings accordingly.

- Similarly, BZDs are indicated for short-term relief (2 to 4 weeks only) of anxiety that is severe, disabling or subjecting an individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness.

- BZDs may also be added to anti-depressants in the short term to offset their initial excitatory effects in the treatment of depression and anxiety disorders and should be tapered and withdrawn by 4 weeks. BZDs should not be used as monotherapy in the treatment of depression.

- BZDs can be used in the management of medical conditions such as seizures, epilepsy and alcohol withdrawal. However, such complicated medical conditions should be referred to tertiary and specialist care.

- BZDs/hypnotics should be avoided in pregnant and breast-feeding women.

- It should also be avoided as first line treatment in children and adolescents, unless being used by specialists for specific indications.

- BZDs/hypnotics should be used with caution in older persons and only on a short-term basis and at a lower dose. Long-term use should be avoided due to the risk of cognitive impairment and falls.

- Care should be taken when prescribing BZDs/hypnotics in certain persons to avoid excessive sedation, which may pose a risk to the patient who drives or operates heavy machinery etc.

Abuse and Dependence

- Extended and long-term use of BZDs/hypnotics beyond 2 to 4 weeks is not recommended even when used at therapeutic doses, because efficacy is not clearly established.
- There must be appropriate clinical review, clear indications and adequate documentation for any continued or repeat BZD/hypnotic prescription.
- The concurrent use of two or more BZDs/hypnotics should be avoided.
- BZD/hypnotic use should be limited to short term symptomatic relief, at the lowest effective dose and taken intermittently, to minimise the side-effects and risks of dependence.
- BZDs should be gradually tapered, monitored and titrated to minimise withdrawal symptoms. For those on less than 4 weeks of BZDs, the dose can be discontinued or reduced over 1 to 2 weeks. For those on more than 4 weeks of BZDs requiring a withdrawal protocol, doctors can refer to the CPG for BZDs or refer to specialist care.
- All patients receiving BZDs/hypnotics should be routinely advised about the risk of developing dependence. Patients receiving BZDs/hypnotics should be advised to obtain all such prescriptions from the same doctor wherever possible, so that the risk of abuse and dependence may be monitored.
- Caution should be exercised when prescribing BZDs/hypnotics or avoided altogether for patients with known history or evidence of alcohol or substance abuse or those with signs of intravenous drug use. Doctors are strongly discouraged from prescribing highly addictive BZDs such as midazolam (Dormium®) and nimetazepam (Erimin®) as they are commonly abused.
- Under Regulation 19 of the Misuse of Drugs Regulation, a doctor who attends to a person who he considers, or has reasonable grounds to suspect, is a drug addict, shall within 7 days of the attendance, furnish to both the Director of Medical Services and the Director of the Central Narcotics Bureau, the particulars of that person.

Documentation

The standard required by the MOH BZD/hypnotic administrative guidelines on the documentation and maintenance of patient medical records states that:

- All information relating to a particular patient must be consolidated as one medical record relating only to that patient. Such information must be **legibly documented**.

- Each patient's medical record must be entirely reproducible upon request by the MOH or SMC.

- The following information must be documented in the medical record of <u>every</u> patient who is prescribed with BZDs/hypnotics:

  - Comprehensive history, including psychosocial history and previous use of BZDs/hypnotics.
  - Comprehensive physical examination findings, including evidence of misuse of BZDs/hypnotics or other drugs.
  - Withdrawal symptoms to BZDs/hypnotics previously experienced by the patient, if any.

- The following information must be documented in the medical records of **every patient each time** he/she is prescribed with BZDs/hypnotics, either initially or as repeat prescriptions:

  - The prescribed type/name of BZD/hypnotic, its dosage and duration of use.
  - Indication(s) and/or justification for prescribing BZDs/hypnotics.
  - Physical signs or evidence of tolerance, physical/psychological dependence or any illicit use or misuse of BZDs/hypnotics or other drugs.

Specialist Referrals

The following patients should not be further prescribed with BZDs/hypnotics, but referred to the appropriate specialist for further management:

- Patients who require or have been prescribed BZDs/hypnotics beyond a cumulative period of 8 weeks.

- Patients who are already on high-dose and/or long-term BZDs from their specialists or general hospitals; where possible, these patients should be referred back to their respective specialists for further management until they are weaned off BZDs/hypnotics.

- Patients who are non-compliant with professional advice or warnings to reduce intake of BZDs/hypnotics.

Patients who refuse to be referred to a specialist should be counselled appropriately. Such refusal should be documented in the patients' medical records. Patients who refuse and turn aggressive should be reported to the police.

Codeine Containing Cough Mixtures (CCCMs)

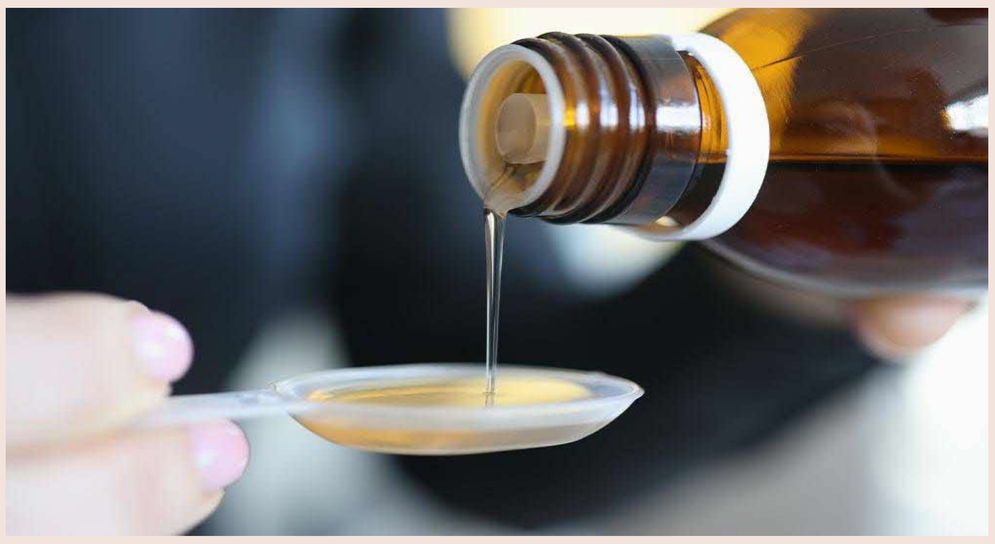
This section on CCCMs takes reference from the following documents:

- The guidelines for the safe prescribing of opioids, April 2021.[3]
- The MOH circular on the revised restrictions on the sale and supply of codeine cough medications, September 2021.[4]

Guidelines on the Use of CCCMs

Codeine in the treatment of refractory cough is a common example of an opioid that is often used for a non-pain indication. It is believed to work primarily on the central nervous system (CNS), causing depression of the cough reflex. **However, despite widespread usage, there is little evidence supporting anti-tussive activity for orally administered codeine. The varying abilities of individuals to metabolise codeine (pro-drug) into morphine (active drug) in the liver, results in unpredictable under-dosing and over-dosing.**

- CCCMs are not recommended as first line treatment of cough in all cases.
- CCCMs should be avoided in pregnant and breastfeeding women.
- Codeine use in any form for any purpose should be avoided in children under 12 years of age. It is recommended for doctors to adhere to HSA's prevailing safety alerts to health care professionals on the recommendations on the use of codeine-containing products for the treatment of pain and the relief of cough and cold in children and adolescents.
- CCCMs should also be used with caution in the following:
  - Geriatric population – due to sedative effects and respiratory depression.
  - Those with other medical issues – especially respiratory, cardiovascular and CNS co-morbidities.



- CCCMs should only be prescribed when all other cough medications have proven ineffective and/or are contraindicated due to allergy or adverse effects.

- Note the addictive potential of pseudoephedrine as well, in combination medications with CCCMs.

- CCCMs should be prescribed at the lowest effective dose, and for the shortest possible duration when indicated.

- Prescription history should be checked using the National Health Electronic Record (NEHR) where available when a CCCM is supplied.

- Patients should be appropriately counselled and educated on the risks of taking long-term CCCMs.

- Doctors must not supply more than the following to any individual **within a period of 7 days:**

  - An aggregate amount of **240 ml of CCCM** when supplied in liquid form.
  - An aggregate amount of **335 mg of codeine** (calculated as codeine base) contained in the cough preparations when supplied in solid form only or in both liquid and solid forms.

- Prescriptions of CCCMs should not be repeated more than 2 consecutive times without a physical consultation to minimise the risk of abuse of diversion.

- Use of CCCMs should be discontinued after a month in view of the increased risk of dependence.

Monitoring is required in use of CCCMs. The following should be looked out for:

Adverse effects
Drowsiness, slowed or shallowed breathing, confusion, hallucinations. The higher the daily dose, the higher the risk of overdose and other adverse effects.

Fitness to drive
Slowed reaction time, drowsiness, clouding of judgement

Opioid misuse, addiction or diversion
Patients with prolonged cough and have used CCCMs daily or almost daily, for more than a month, have a high likelihood of drug dependence.

Doctors should look out for behaviours indicative of opioid misuse/abuse:

- Self-administering increasing doses of opioids
- Obtaining additional opioids from other doctors
- Purposeful sedation
- Early request for refills
- Misplacing prescriptions

Documentation

Clinical notes when cough medication is prescribed should include:

- Duration of cough – Acute, Sub-acute or Chronic
- Associated symptoms, their duration and time course (current and/or previous)
- Red Flags
- Relevant past history in sub-acute and chronic cough:
  - Respiratory and other medical conditions
  - Drugs and medication
  - Smoking
  - Occupation and environmental factors
- Details of investigations and previous treatment.

In addition, when CCCMs are prescribed, the notes should include the following, with information obtained from the NEHR where possible:

- Strength, dosage and duration of use of the CCCM
- Indications and justification of the CCCM
- Past history of substance abuse – codeine/opioids, alcohol, BZDs, controlled drugs
- Recent CCCM prescriptions from other medical institutions
- Findings from assessment for mental health problems – anxiety, depression
- Relevant physical examinations – ENT, respiratory, cervical lymph nodes
- Relevant significant negatives for specific diseases

Specialist Referral

- Patients should be referred to a respiratory specialist if cough persists for more than 8 weeks or remains undiagnosed after all red flags have been considered and relevant investigations completed.

- Patients that show evidence of misuse, abuse and dependence on CCCMs should not be prescribed further doses, but referred to a specialist for further management.

- The same general principles that apply to BZDs/hypnotics with respect to refusal for referral, should also apply to CCCMs - namely counselling, documentation and management of aggressive patients.

References
1. MOH Clinical Practice Guidelines 2/2008 – Prescribing of Benzodiazepines.
2. Administrative Guidelines on the prescribing of benzodiazepines and other hypnotics, MH 70:41/24 Vole 3. 14 October 2008.
3. National guidelines for the safe prescribing of Opioids 2021; Section 5, April 2021.
4. Revised restrictions on the sale and supply of codeine cough preparations. MOH Circular No. 134/2021.