CDC Opioid Guideline Update, Opioid Management, and Opioid Alternatives

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CSHP

CSHP SEMINAR 2016 TRANSITIONS IN PHARMACY

DISCLOSURE STATEMENT:
I nor my family have any significant financial relationships with any commercial interests that might bias the information given today during my presentation

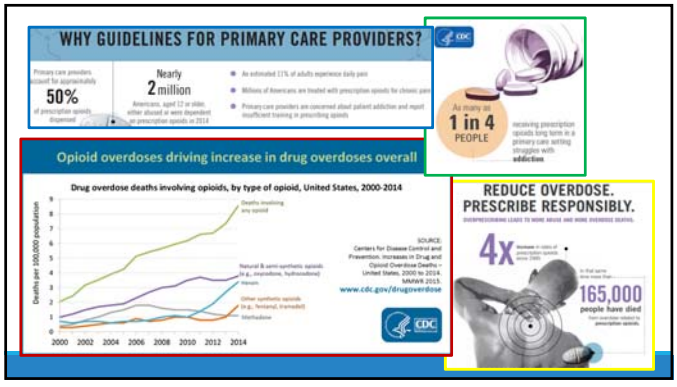
This educational activity has not received commercial support

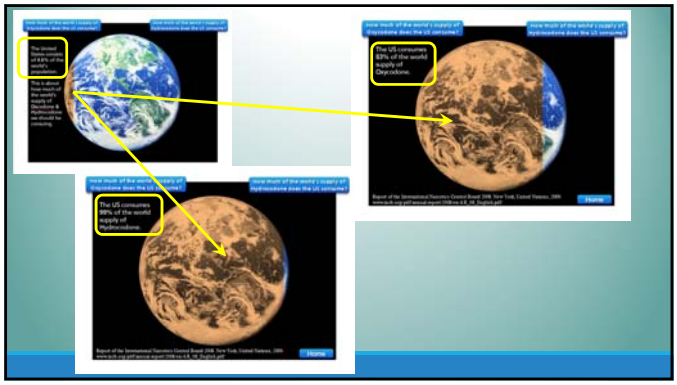
Disclaimer……

The medications and treatment considerations covered in certain sections of this presentation are not all inclusive and simply provide a look at some of the medication management practices, at a local level, within the Kaiser Permanente Riverside Service Area

Test Questions

1. What is the approximate MME of fentanyl patch 25mcg/hr?
   a) 50 MME
   b) 100 MME
   c) 60 MME
   d) 37.5 MME
2. Which of the following would generally NOT be considered a red flag for opioid abuse/misuse?
   a) Losing medication
   b) Doctor shopping
   c) Urine drug screen negative for prescribed opioid
   d) Calling in for a refill 2 days before the prescription is due





2016 CDC Opioid Guideline Highlights
(excludes cancer, palliative, end-of-life care)

- Nonpharmacologic and nonopioid therapy first
- Establish treatment goals
- Discuss risks/benefits of opioids
- If starting opioids, use immediate-release opioids instead of extended-release opioids/long-acting opioids

2016 CDC Opioid Guideline Highlights
(excludes cancer, palliative, end-of-life care)

- Review patient's controlled substance prescription history
- Urine Drug Screen (UDS)
- Avoid concurrent use of opioids and benzodiazepines
- Evidence-based treatment for patients with opioid use disorder

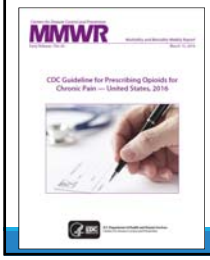
2016 CDC Opioid Guideline Highlights

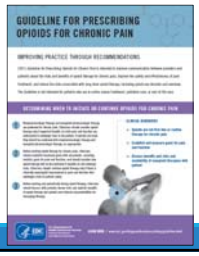
(excludes cancer, palliative, end-of-life care)

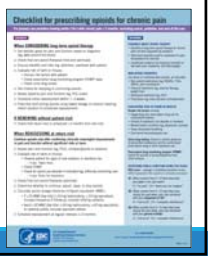
- Reassess risk/benefits before increasing dose >50 MME/day
- Avoid increasing dose >90 MME/day
- For acute pain, prescribe the lowest effective dose and do not prescribe greater quantity than needed
- Re-evaluate risks/benefits within 1 to 4 weeks of initiation/escalation and then at least every 3 months thereafter
- Consider naloxone for patients at higher risk for overdose

For more information and tools visit http://www.cdc.gov/drugoverdose

- Guidelines for Prescribing Opioids for Chronic Pain
- Prescribing Checklist
- Tapering Guide
- Non-opioid alternatives
- Additional tools/resources







Definitions

Opioid
- All agonists and antagonists with morphine-like activity and can be naturally occurring or synthetic opioid peptides

Opiate
- Applies to drugs derived from opium including both natural products (eg. morphine, codeine) and semisynthetic congeners derived from them

Narcotic
- A drug derived from opium or opium-like compounds, with potent analgesic effects, that has the potential for dependence and tolerance following repeated dosing

Definitions

Addiction
- Aberrant use of substance, including loss of control, compulsive use, preoccupation, and continued use despite causing physical, mental, or social harm

Pseudoaddiction
- An iatrogenic syndrome where a patient may exhibit certain addictive type behaviors due to undertreatment of pain. Distinguished from addiction in that behaviors typically resolve once pain is effectively treated

Physical Dependence
- The physiological adaptation of the body to the presence of an opioid. It is defined by the development of withdrawal symptoms when opioids are discontinued, when the dose is reduced abruptly, or when an antagonist/agonist-antagonist is administered

Tolerance
- A state of pharmacologic adaptation which requires and increased amount of drug to produce the same effect or a reduced effect is observed if the dose is unchanged

Goals of Chronic Pain Management

- Decrease pain level
- Functional improvement
- Minimize potential medication side effects
- Emphasize non-pharmacologic tools
- Individualize management to each patient and patient's response

Chronic Pain Management Clinical Pearls

- Medication is only ¼ of the treatment "pie"
  - Meds: maximize analgesia/function and minimize side effects
  - Activity modification
  - Body mechanics
  - Managing mental health and general wellness
- You should NOT be working harder than the patient
  - Emphasize self-care
- Set realistic goals with patient
  - Cure? Pain-free?
- Multi-modal approach
- Emphasize non-pharmacologic treatments
- Adjuvant medications are key

Interdisciplinary Committees And Pain Pharmacist

Pain Pharmacist

- Manage opioid tapers
- Track progress
- Physician education
- Patient education – CBTR
- Treatment coordination

Interdisciplinary Committees

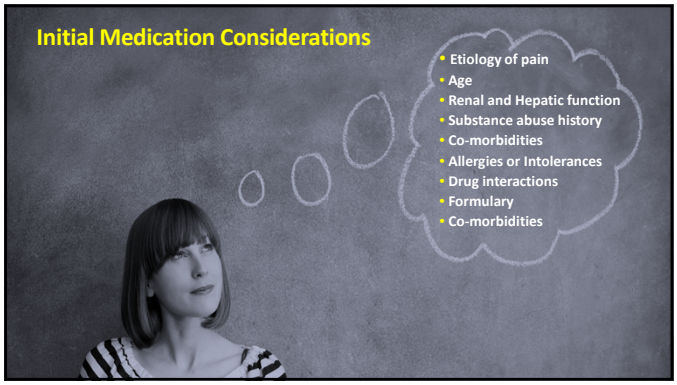
- Triage high risk patients
- Assess/Track progress
- Physician education
- Assist physicians with complicated patient cases
- Development of policies, protocols, practice recommendations

Standardized Tools

Non-Pharmacologic Management of Chronic Pain

- Pacing
- Heat/Ice
- Deep breathing
- Guided imagery
- Distraction
- Cognitive Behavioral Therapy & Rehabilitation (CBTR)
- Physical Therapy
- Acupuncture
- TENS unit
- Exercise/movement

Initial Medication Considerations



- Etiology of pain
- Age
- Renal and Hepatic function
- Substance abuse history
- Co-morbidities
- Allergies or Intolerances
- Drug interactions
- Formulary
- Co-morbidities

Acetaminophen (APAP)

- Analgesic and antipyretic properties
- No appreciable anti-inflammatory effects
- Avoid or use with caution in hepatic impairment and/or alcohol use

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- Analgesic, antipyretic, and anti-inflammatory properties
- Black Box Warnings
  - Cardiovascular events
  - Treatment of peri-op pain in setting of CABG
  - GI events
- Warnings/Precautions
  - Cardiovascular events
  - GI events
  - CABG surgery
  - Hypertension
  - Hepatic impairment
  - Renal impairment

Topicals

- Capsaicin
- Salicylates
- Menthol
- Topical anesthetics
- NSAIDs
- Compounded creams/gels

Antidepressants: TCAs

- Secondary Amines: Nortriptyline, Desipramine
- Tertiary Amines: Amitriptyline, Doxepin
- May be considered for neuropathic pain
- Dosing – generally requires titration
- Side effects
  - Anticholinergic effects
  - Orthostatic hypotension
  - Sedation
  - Weight gain
  - QT prolongation
- Cautions
  - Use of MAOI within 14 days
  - Acute recovery phase of MI
  - Elderly
  - Drug interactions
  - Suicidal thinking/behavior

Antidepressants: SNRIs

- Venlafaxine (Effexor ®), Duloxetine (Cymbalta ®)
- May be considered for neuropathic pain
- Dosing – generally requires titration
- Side effects
  - HA
  - Somnolence/dizziness
  - Insomnia
  - Hypertension
  - Tachycardia
- Cautions (Venlafaxine)
  - Use of MAOI within 14 days
  - Renal or hepatic impairment
  - Suicidal thinking/behavior
  - Cardiovascular disease: hypertension/tachycardia
  - Drug interactions

Anticonvulsants

- Gabapentin (Neurontin ®), Topiramate (Topamax ®), Pregabalin (Lyrica ®)
- Used for neuropathic pain

Gabapentin

- Dosing: consider starting at 100-300mg at bedtime and slow titration at weekly intervals to max of 3600mg/day
- Side effects
  - Fatigue
  - Somnolence
  - Dizziness
  - Peripheral edema
- Cautions
  - Renal impairment
  - Titrate slowly in elderly

Skeletal Muscle Relaxants (SMRs)

- Tizanidine (Zanaflex ®), Baclofen (Lioresal ®), Methocarbamol (Robaxin ®), Cyclobenzaprine (Flexeril ®), Metaxalone (Skelaxin ®)
- May be useful for muscle spasm/spasticity and myofascial pain
- Side effects: In general, all may cause sedation and muscle weakness
- Avoid in the elderly

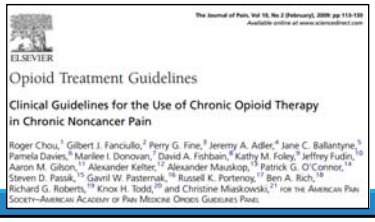
Opioids

- Alkaloids derived from opium
- Natural and synthetic agents
  - Mimicks naturally occurring substances
- 3 major chemical classes
  - Phenanthrenes: morphine, codeine, hydrocodone, hydromorphone, oxycodone, oxymorphone
  - Phenylpiperidines: meperidine, fentanyl
  - Diphenylheptanes: methadone, propoxyphene

American Pain Society – American Academy of Pain Medicine Opioid Guidelines

2009

"By panel consensus, a reasonable definition for high dose opioid therapy is >200mg daily of oral morphine (or equivalent), based on maximum opioid doses studied in randomized trials and average opioid doses observed in observational studies"


ELSEVIER

Opioid Treatment Guidelines

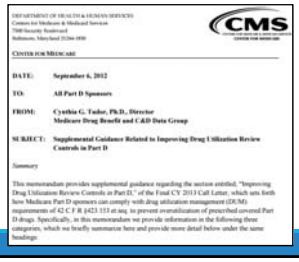
Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain

Centers for Medicare and Medicaid Services (CMS)

2012

CMS released memo addressing the public health concern surrounding potential opioid overutilization

- **Effort to improve the safe and effective use of opioids in Medicare Part D**
- **Daily morphine equivalent dose (MED) above 120mg for at least 90 consecutive days w/ >3 prescribers and >3 pharmacies**


CMS

CENTER FOR MEDICARE

DATE: September 6, 2012

TO: All Part D Sponsors

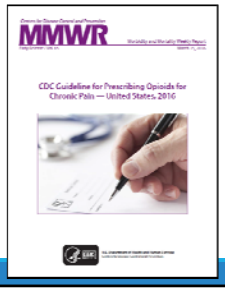
FROM: Cynthia G. Tudor, Ph.D., Director
Medicare Drug Benefit and C&D Data Group

SUBJECT: Supplemental Guidance Related to Improving Drug Utilization Review Controls in Part D

CDC's Guideline for Prescribing Opioids for Chronic Pain

2016

Earlier this year the CDC released new opioid guidelines that further reduced the recommended dose of opioids to <90 MME/day



US Surgeon General Letter to all US Physicians

2016

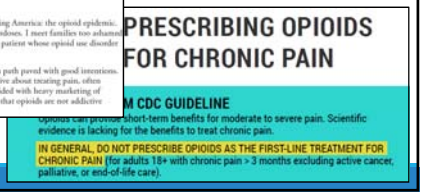
UNITED STATES SURGEON GENERAL
Vivek H. Murthy, M.D., M.B.A.

August 2016

Dear Colleague,

I am asking for your help to solve an urgent health crisis facing America: the opioid epidemic. Everywhere I travel, I see communities devastated by opioid overdoses. I meet families too ashamed to seek treatment for addiction. And I will never forget my own patient whose opioid use disorder began with a course of morphine after a routine procedure.

It is important to recognize that we arrived at this place on a path paved with good intentions. Nearly two decades ago, we were encouraged to be more aggressive about treating pain, often without enough training and support to do so safely. This coincided with heavy marketing of opioids to doctors. Many of us were even taught – incorrectly – that opioids are not addictive when prescribed for legitimate pain.



PRESCRIBING OPIOIDS FOR CHRONIC PAIN

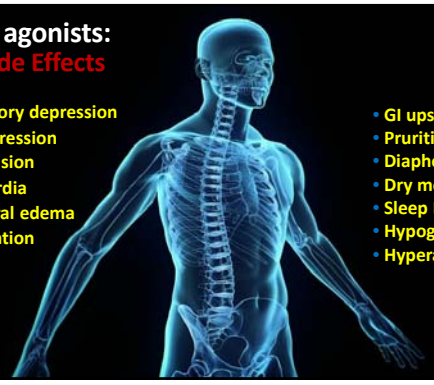
M CDC GUIDELINE

short-term benefits for moderate to severe pain. Scientific evidence is lacking for the benefits to treat chronic pain.

IN GENERAL, DO NOT PRESCRIBE OPIOIDS AS THE FIRST-LINE TREATMENT FOR CHRONIC PAIN (for adults 18+ with chronic pain > 3 months excluding active cancer, palliative, or end-of-life care).

Opioid agonists: Class Side Effects

- Respiratory depression
- CNS depression
- Hypotension
- Bradycardia
- Peripheral edema
- Constipation



- GI upset
- Pruritis
- Diaphoresis
- Dry mouth
- Sleep Disorders
- Hypogonadism
- Hyperalgesia

Opioid Agonists: Morphine, Oxycodone, Hydrocodone, Hydromorphone

- In general, similar pharmacokinetic and side effect profile
- Different metabolite profile:

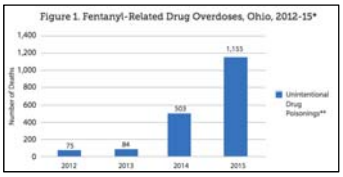
- Morphine - 2 major metabolites
  - ~75% metabolized to morphine-3-glucuronide
    - Lacks analgesic effect but may cause neurotoxicity
  - ~5%-10% metabolized to morphine-6-glucuronide
    - Considered more potent analgesic than parent compound
- Oxycodone - 2 major metabolites
  - Oxymorphone
    - Potent analgesic but typically low plasma concentrations
  - Noroxycodone
    - Weak analgesic
- Hydromorphone - many major/minor metabolites
  - Hydromorphone-3-glucuronide
    - May cause neuroexcitatory effects
  - Hydromorphone-6-glucuronide
    - Accumulation may lead to myoclonus, agitation, and seizure
- Hydrocodone - 2 major metabolites
  - Hydromorphone
    - Much greater affinity for mu receptor than parent compound
  - Norhydrocodone

Opioid Agonist: Tramadol

- Effective 8/18/14, DEA reclassified tramadol as a Schedule IV controlled substance
- 2 primary MOA
  - Mu receptor agonist
  - Inhibits re-uptake of serotonin and norepinephrine
- Active metabolite (O-desmethyl tramadol) t1/2 ~ 7-9 hours
- Cautions
  - Seizure disorder
  - Drug interactions
  - Falls

Opioid Agonist: Fentanyl

- Per CDC recommendations, only clinicians familiar with the dosing and absorption properties should consider prescribing it
- Fentanyl 25mcg/hr patch is ~equivalent to 60 MME/day
- Inactive metabolites
- May be useful in opioid TOLERANT patient's with morphine allergy
- Contraindicated in opioid naïve patients
- Cautions
  - Proper disposal of patch to prevent accidental exposure
  - Administration issues



Opioid Agonist: Methadone

- Per CDC recommendations, should not be the first choice for a long-acting opioid and should only be used by clinicians familiar with methadone and it's unique properties
- Multiple MOA
  - Mu receptor agonist
  - NMDA receptor antagonist
  - Inhibits re-uptake of serotonin and norepinephrine
- Long and variable t1/2
  - Elimination half-life is considerably longer than the half-life of analgesia
    - Side effect profile can persist well beyond duration of analgesia
- Cautions
  - QT prolongation
  - Generally not recommended for breakthrough pain due to long half-life and variable pharmacokinetics
  - Detox/Maintenance restricted to Opioid Treatment Programs

Opioid Agonists to Avoid……in General

Darvocet
- Withdrawn from market d/t cardiac effects

Demerol
- Recommended to limit use by most regulatory bodies
- Beers List

Codeine
- Some patients are unable to convert codeine to morphine for analgesic effect

Opioid Prescribing Pearls

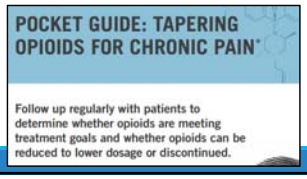
- Ensure legitimate diagnosis
- Recommend history and physical exam prior to opioid trial
- Document 5 A's
  - Analgesia
  - Activity (function)
  - Adverse effects
  - Aberrant behaviors
  - Affect
- Maximize non-pharmacologic and non-opioid therapy first
- Do not write range orders or PRN orders for long-acting opioids

Opioid Prescribing Pearls

- For chronic opioid patients limit supply to 30 days with no refills
- Opioid agreements
- Urine Drug Screens
  - Drugs of abuse and opioid screens
- Pill counts randomly and for aberrant behavior
- CURES reports

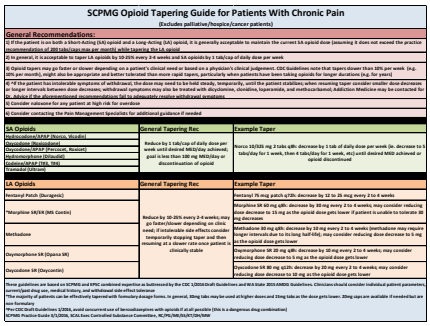
CDC Opioid Tapering Recommendations

- Decrease 10% per week
- Coordinate with specialists/experts prn
- Psychosocial support
- Adjust the rate/duration of taper based on patient's response
- Don't reverse the taper; slow/pause the rate and manage withdrawal symptoms
- Consider extending dosing interval once smallest available dose is reached



SCPMG Opioid Tapering Guide

- Created prior to official CDC guidelines
- Reduce opioid dose by 10-25% every 2 to 4 weeks
- Tapers may go faster or slower depending clinical need
- Consider naloxone for any high risk patient



SCPMG Opioid Tapering Guide for Patients With Chronic Pain

(Excludes palliative/hospice/cancer patients)

General Recommendations:

i) If the patient is on both a Short-Acting (SA) opioid and a Long-Acting (LA) opioid, it is generally acceptable to maintain the current SA opioid dose (assuming it does not exceed the practice recommendation of 200 tabs/caps mg per month) while tapering the LA opioid

ii) In general, it is acceptable to taper LA opioids by 10-25% every 2-4 weeks and SA opioids by 1 tab/cap of daily dose per week

iii) Opioid tapers may go faster or slower depending on a patient's clinical need or based on a physician's clinical judgement. CDC Guidelines note that tapers slower than 10% per week (e.g. 10% per month), might also be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g. for years)

iv) *If the patient has intolerable symptoms of withdrawal, the dose may need to be held steady, temporarily, until the patient stabilizes; when resuming taper consider smaller dose decreases or longer intervals between dose decreases; withdrawal symptoms may also be treated with dicyclomine, clonidine, loperamide, and methocarbamol; Addiction Medicine may be contacted for ex. Advice if the aforementioned recommendations fail to adequately resolve withdrawal symptoms

v) Consider naloxone for any patient at high risk for overdose

vi) Consider contacting the Pain Management Specialists for additional guidance if needed

SA Opioids	General Tapering Rec	Example Taper
Hydrocodone/APAP (Norco, Vicodin)	Reduce by 1 tab/cap of daily dose per week until desired MED/day achieved; goal is less than 100 mg MED/day or discontinuation of opioid	Norco 10/325 mg: 2 tabs q8h: decrease by 1 tab of daily dose per week (ie. decrease to 5 tabs/day for 1 week, then 4 tabs/day for 1 week, etc) until desired MED achieved or opioid discontinued
Oxycodone/APAP (Percocet, Roxicet)		
Hydromorphone (Dilaudid)		
Codeine/APAP (T#3, T#4)		
Tramadol (Ultram)		

LA Opioids	General Tapering Rec	Example Taper
Fentanyl Patch (Duragesic)	Reduce by 10-25% every 2-4 weeks; may go faster/slower depending on clinical need; if intolerable side effects consider temporarily stopping taper and then resuming at a slower rate once patient is clinically stable	Fentanyl 75 mcg patch q72h: decrease by 12 to 25 mcg every 2 to 4 weeks
*Morphine SR/ER (MS Contin)		Morphine SR 60 mg q8h: decrease by 30 mg every 2 to 4 weeks; may consider reducing dose decrease to 15 mg as the opioid dose gets lower if patient is unable to tolerate 30 mg decrease
Methadone		Methadone 80 mg q8h: decrease by 10 mg every 2 to 4 weeks (methadone may require longer intervals due to its long half-life); may consider reducing dose decrease to 5 mg as the opioid dose gets lower
Oxymorphone SR (Opana SR)		Oxymorphone SR 20 mg q8h: decrease by 10 mg every 2 to 4 weeks; may consider reducing dose decrease to 5 mg as the opioid dose gets lower
Oxycodone SR (Oxycontin)		Oxycodone SR 80 mg q12h: decrease by 20 mg every 2 to 4 weeks; may consider reducing dose decrease to 10 mg as the opioid dose gets lower

These guidelines are based on SCPMG and KPSC combined expertise as buttressed by the CDC 3/2016 Draft Guidelines and WA State 2015 AMDG Guidelines. Clinicians should consider individual patient parameters, current/past drug use, medical history, and withdrawal side effect tolerance

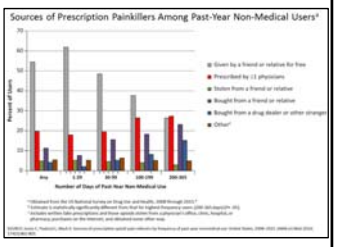
The majority of patients can be effectively tapered with formulary dosage forms. In general, 30mg tabs may be used at higher doses and 10mg tabs as the dose gets lower. 20mg caps are available if needed but are non-formulary

*Per CDC Draft Guidelines 1/2016, avoid concurrent use of benzodiazepines with opioids if at all possible (this is a dangerous drug combination)

SCPMG Practice Guide 6/1/2016, SCAL Exec Controlled Substance Committee, KC/PN/NR/DS/RT/DN/MM

Red Flags for Opioid Abuse

- Early refills - overuse, lost/stolen prescriptions, frequent "vacations"
- Requesting med changes constantly….. "nothing works"
- Requesting specific medications, brand name medications, or certain color medications
- Doctor shopping
- Paying cash
- Refusing imaging or other work-up
- Refusing lab tests
- Urine drug screen inconsistencies



Opioid Rotations

May help overcome tolerance and opioid-induced hyperalgesia
- May have less utility now with lower MME recommendations from CDC

May help minimize or eliminate certain side effects

Recommend to reduce new opioid dose by 25% to 75% to account for incomplete cross tolerance

May consider either cross-titrating or a stop-start approach
- Stop-start approach may be beneficial in patients with poor medication compliance, cognitive deficits, or unable to follow instructions

Test Questions (answers in red)

1. What is the approximate MME of fentanyl patch 25mcg/hr?
   a) 50 MME
   b) 100 MME
   c) 60 MME
   d) 37.5 MME
2. Which of the following would generally NOT be considered a red flag for opioid abuse/misuse?
   a) Losing medication
   b) Doctor shopping
   c) Urine drug screen negative for prescribed opioid
   d) Calling in for a refill 2 days before the prescription is due

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