PRAIRIE MOUNTAIN HEALTH

Clinical Case of Symptom Management and Deprescribing

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Geriatric Oncology Day

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Presenter Disclosure

Name: Elizabeth Rhynold MD FRCPC

Relationships with commercial interests:

- Grants/Research Support: Dr. John Wade Patient Safety Initiatives Grant, Manitoba Institute for Patient Safety
- Speakers Bureau/Honoraria: nil
- Consulting Fees: nil
- Other: Consultant Geriatrician working in Prairie Mountain Health

Mitigating Potential Bias

- Not Applicable

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Learning Objectives

By the end of the session participants will be able to:

- Incorporate self-medication with OTC's into ongoing medication review
- Describe risks associated with common OTC medications
- Recognize the deliriogenic side effects of many medications for symptom management
- Actively plan for deprescribing of symptom management initiated during treatment

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Mrs. R. a great referral!

Thank you for seeing [redacted] a 74 year old female who lives alone in a house in [redacted] has limited supports, (well, acutually no supports) and does not seem to be doing well.
She was diagnosed with endometrial ca stage IIIB in July and is currently recieving chemotherapy in [redacted].
She spends much of her time in hospital between her chemotherpay treatments with complaints of weakness, fatigue and not being able to cope.
She most recently was admitted to [redacted] following her 3rd chemo treatment.
She has been refusing home care, has been refusing an OT assessment.
EMS who has gone to her house several times have expressed concern regarding the states of her house in regards to hygiene and safety.

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Mrs. R.

- Since starting carboplatin + paclitaxel 3 months ago
  - Nausea – dexamethasone 16 mg x 2 days post, aprepitant 80 mg x 2 days post, metoclopramide 5 mg, 6 per day (trial and not renewed)
  - Anxiety – lorazepam 1 mg BID
  - Pain 1st MTP and left knee – ibuprofen 200 q 2 hours*
  - UTI – three courses of nitrofurantoin
  - GI – omeprazole 20 mg daily
- Other chronic medications:
  - Levothyroxine 100 mcg daily (filled 2 months ago after 3 month gap, TSH ↑)
  - Venlafaxine XR 150 daily (1 month ago increased)
  - Perindopril 4 mg/ indapamide 1.25 mg discontinued after first course of chemo

* Ibeuprofen use is the only information not available in eChart

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Mrs. R. CGA highlights

- Cancer diagnosed during psychiatric admission
- No primary care at time of discharge from psychiatric facility (in fact going to SK to see someone intermittently)
- First chemotherapy in Winnipeg. First communication from Cancer Care to local primary care day of cycle #2. This summarized the need for admission a few days following cycle #1 for “profound fatigue, dehydration, confusion and weakness”
- Car accident 10 days after cycle #2 and no longer allowed to drive, living in a small town 30 minutes from urban centre

Mrs. R. CGA highlights

- Functional independence:
  - “Independent” at baseline
  - For 3 days after chemo she sleeps on the couch
  - For those 3 days her cognition was acutely different after cycles 1 & 2
  - For 6 – 7 days after chemo she can’t transfer to the bathroom
  - For 3 weeks post-chemo she can’t clean her house
  - For 3 weeks she is cognitively overwhelmed and can’t problem solve
  - She had falls including hitting her head one week after cycle #2
  - She was fitted for a wheelchair by OT before cycle #3
- O/E 3 ½ weeks post chemo:
  - lying blood pressure 150/100; standing 80/60
- MMSE 3 ½ weeks post chemo:
  - 29/30; no cognitive screening available from acute care or psychiatric stay

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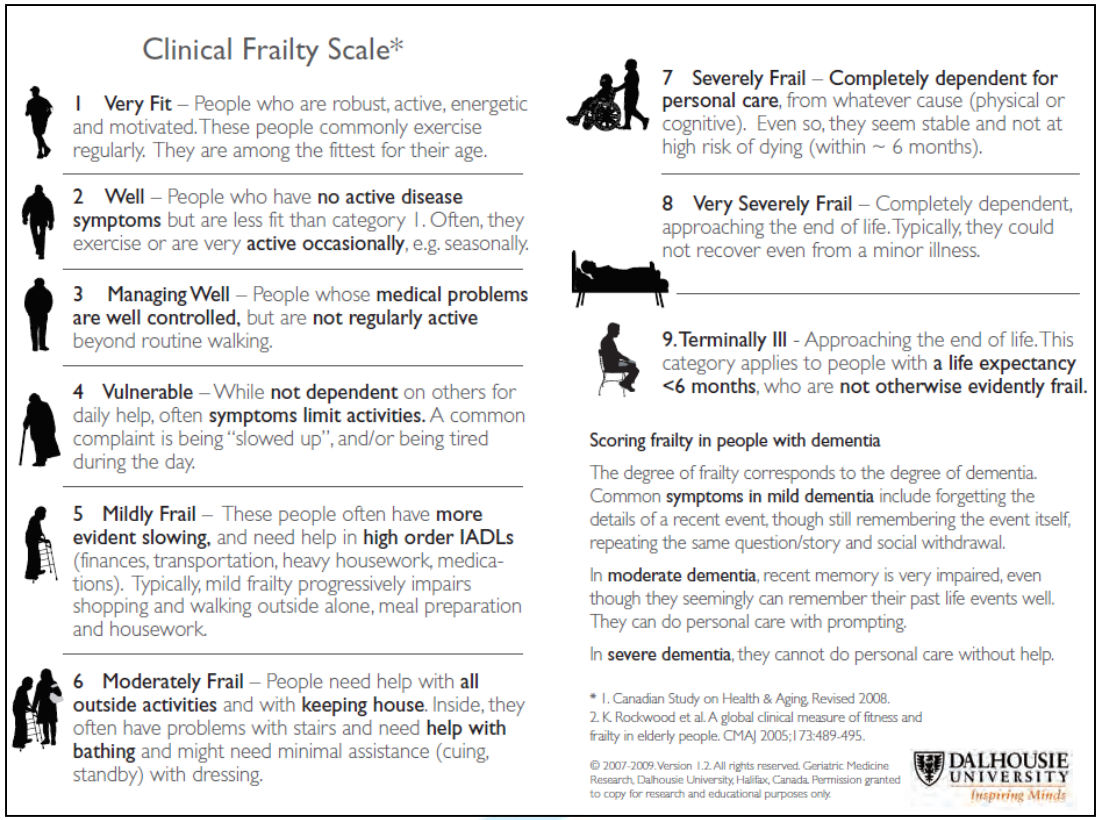
Triaging scarce resources

- The lack of primary care and referral from long-stay inpatient unit
- Living alone
- Mrs. R. is moderately frail in the week following her chemotherapy (dependent for her ADLs)
- She is mildly frail for 3 weeks following her chemotherapy (dependent for IADLs)



Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

DALHOUSIE UNIVERSITY Inspiring Minds

1. Canadian Study on Health & Aging, Revised 2008.

2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Medication review

- **Adam Rose, JAMA 2017 "What is needed is not merely a reconciled list, but the correct medication list."**

Source of information	Details
eChart	Fill history, look back at recent years
Referral letter and other clinician lists	If not taking a medication listed, ask why
Home care client with medication supervision	Medications reconciled every 6 months
The "bag of pill bottles"	
Non-oral medications	Puffers/nebules, topicals, eye drops, nasal sprays, injections
As needed medications	
Symptom specific	What helps, what is being used

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Medication reconciliation

- Kristi Hofer, Senior Pharmacist – Operations states the CCMB electronic patient record will flag interactions when prescribing chemo/supportive care drugs “if the patient’s home medications have been entered appropriately through the medication reconciliation process”
  - CCMB prints DPIN and medications are entered before first appointment
  - First appointment primary nurse clarifies list
  - Oncologists have the option for screening chemo orders with medication history
  - Pharmacist checking chemo order checks for interactions with chemo drugs not with between home meds
  - Future state: patient is provided with a copy of the med list including home meds, chemo and supportive care drugs

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Over-the-counter (OTC) medications

Common symptoms self-treated with OTC's

- Pain

- Sleep
- Nausea
- Diarrhea
- Itch

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Over-the-counter (OTC) medications

Common symptoms self-treated with OTC's

- Pain – drug interactions

- Sleep
- Nausea
- Diarrhea
- Itch

} Anticholinergic

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Over-the-counter (OTC) medications

Common symptoms self-treated with OTC's

- Pain
  - Acetaminophen is a common "geriatric" recommendation. For frail people the recommended daily maximum is often lower (3250 mg Geri-RxFiles Pain Management in Older Adults)
  - Mrs. R stated she was told by her cancer doctor she absolutely cannot take acetaminophen. If this is the case it likely should be in CancerCare letters
  - When I looked up interactions none were identified

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Over-the-counter (OTC) medications NSAIDs

Common symptoms self-treated with OTC's

- Pain
  - NSAIDs are readily available over-the-counter and people will have years of experience taking them
  - MicroMedex was the resource I used to look for drug interactions. Now I will likely be running UpToDate Lexicomp Drug Interactions

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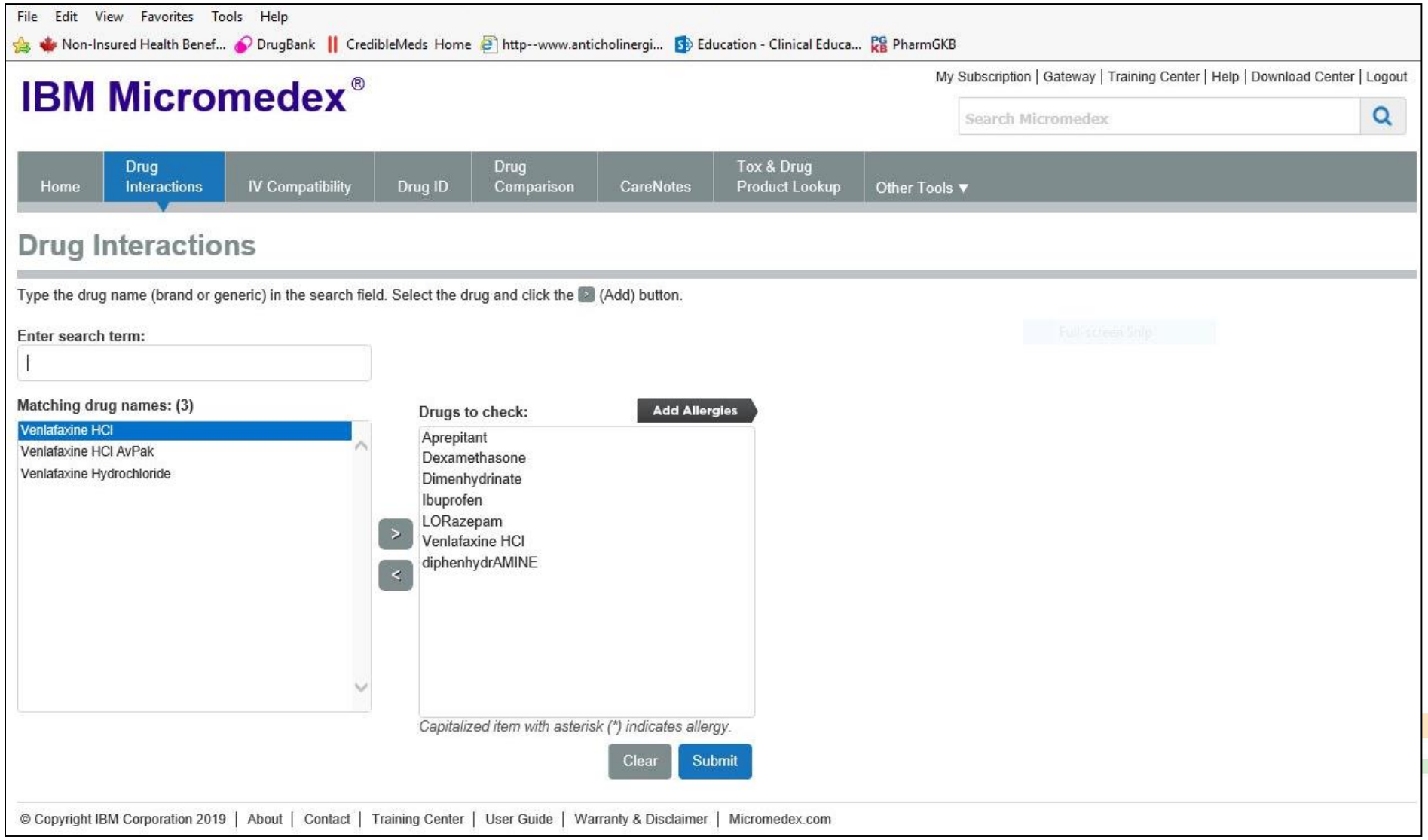
Over-the-counter (OTC) medications NSAIDs



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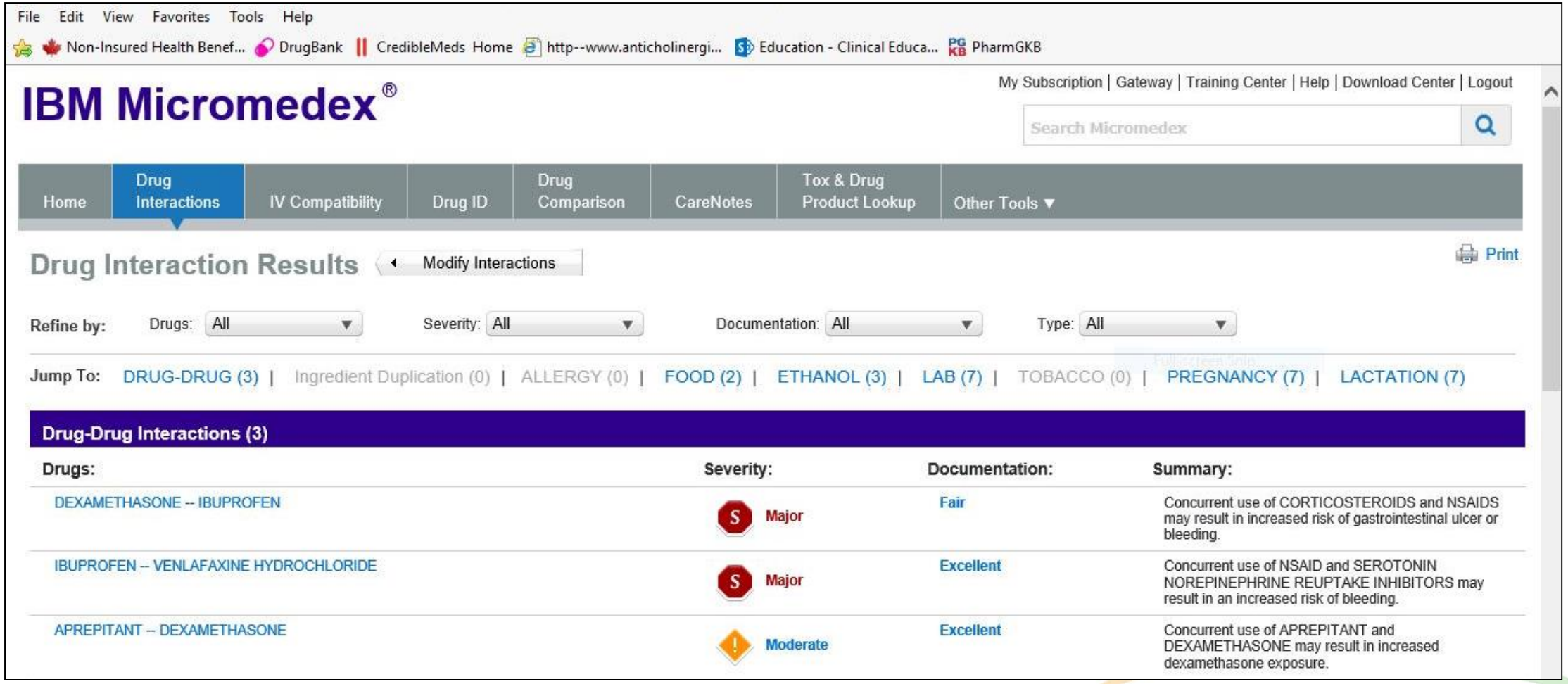
Over-the-counter (OTC) medications NSAIDs



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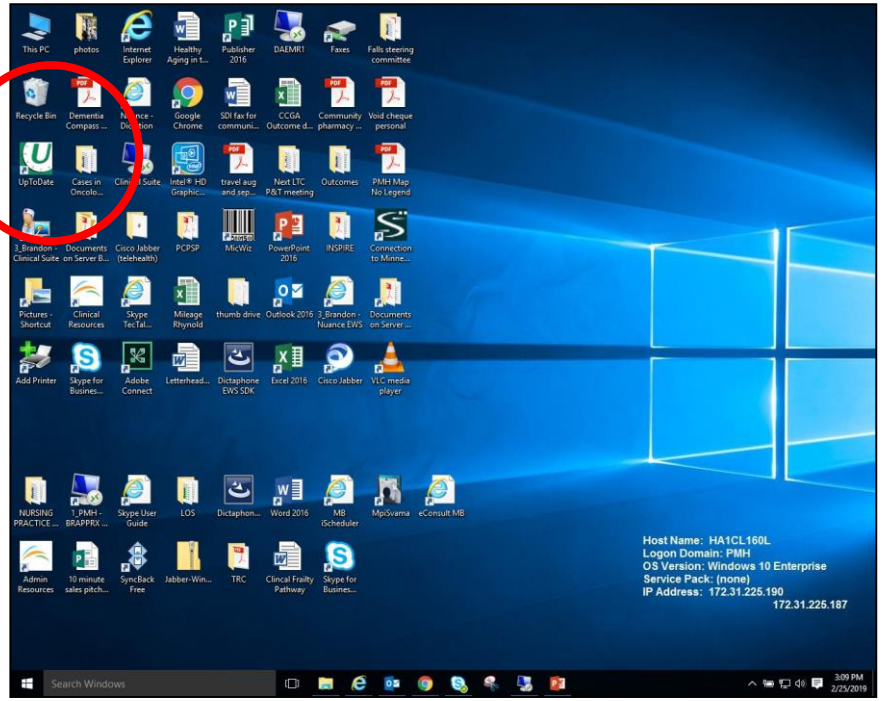
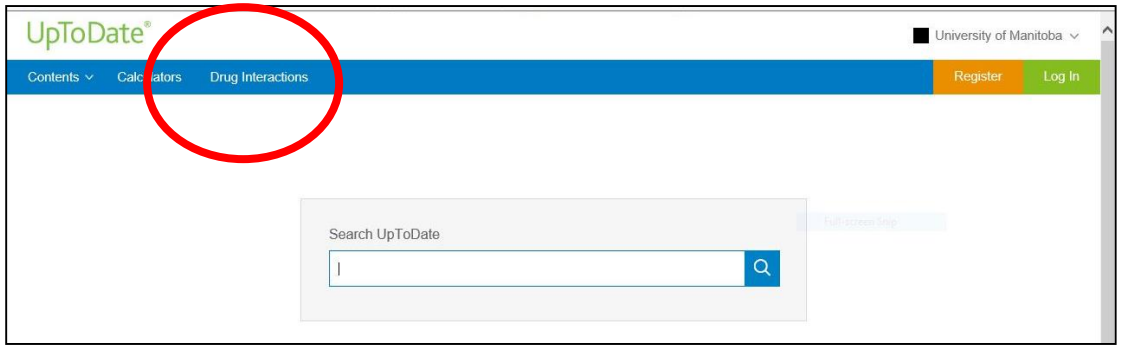
Over-the-counter (OTC) medications NSAIDs





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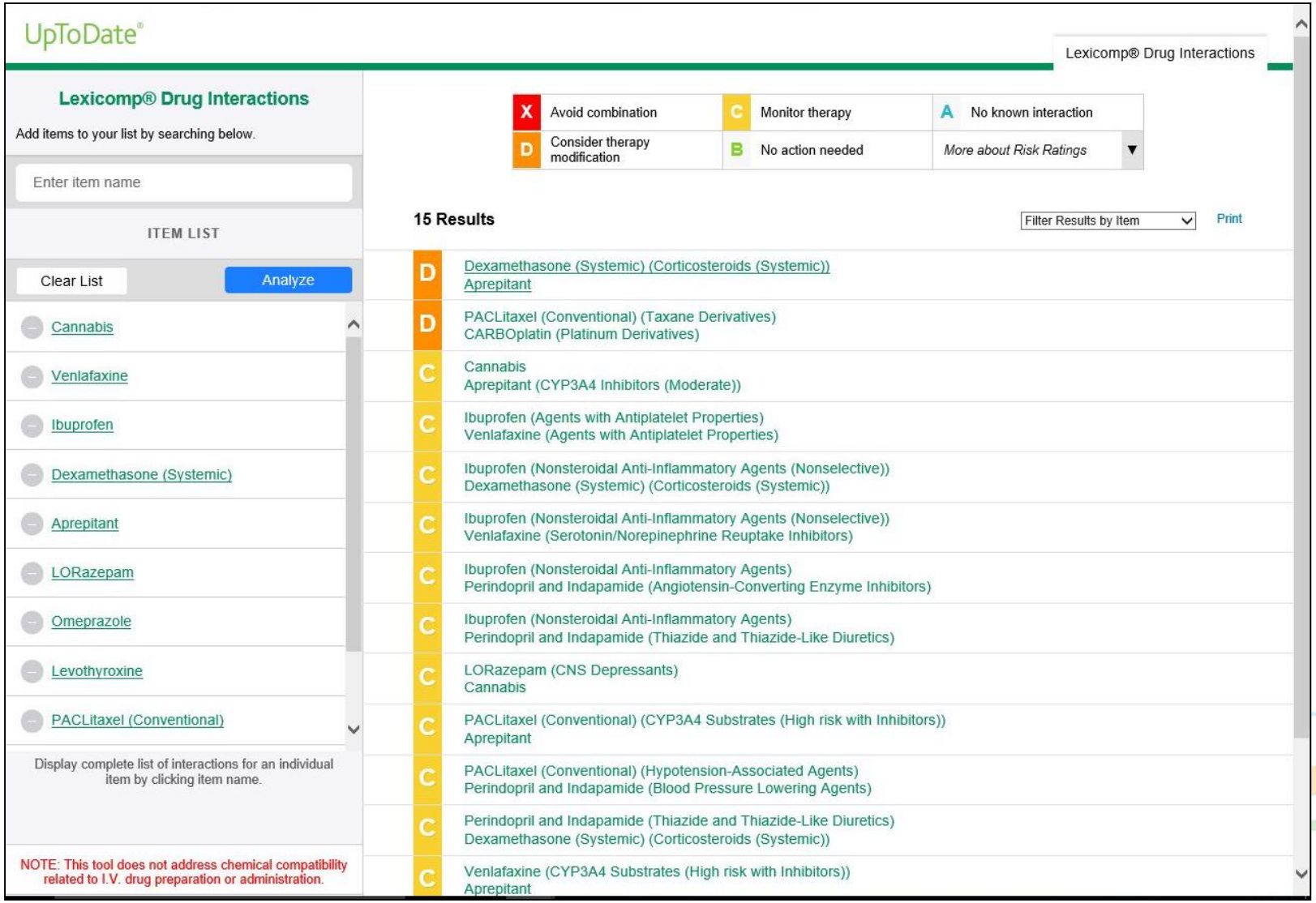
Over-the-counter (OTC) medications NSAIDs



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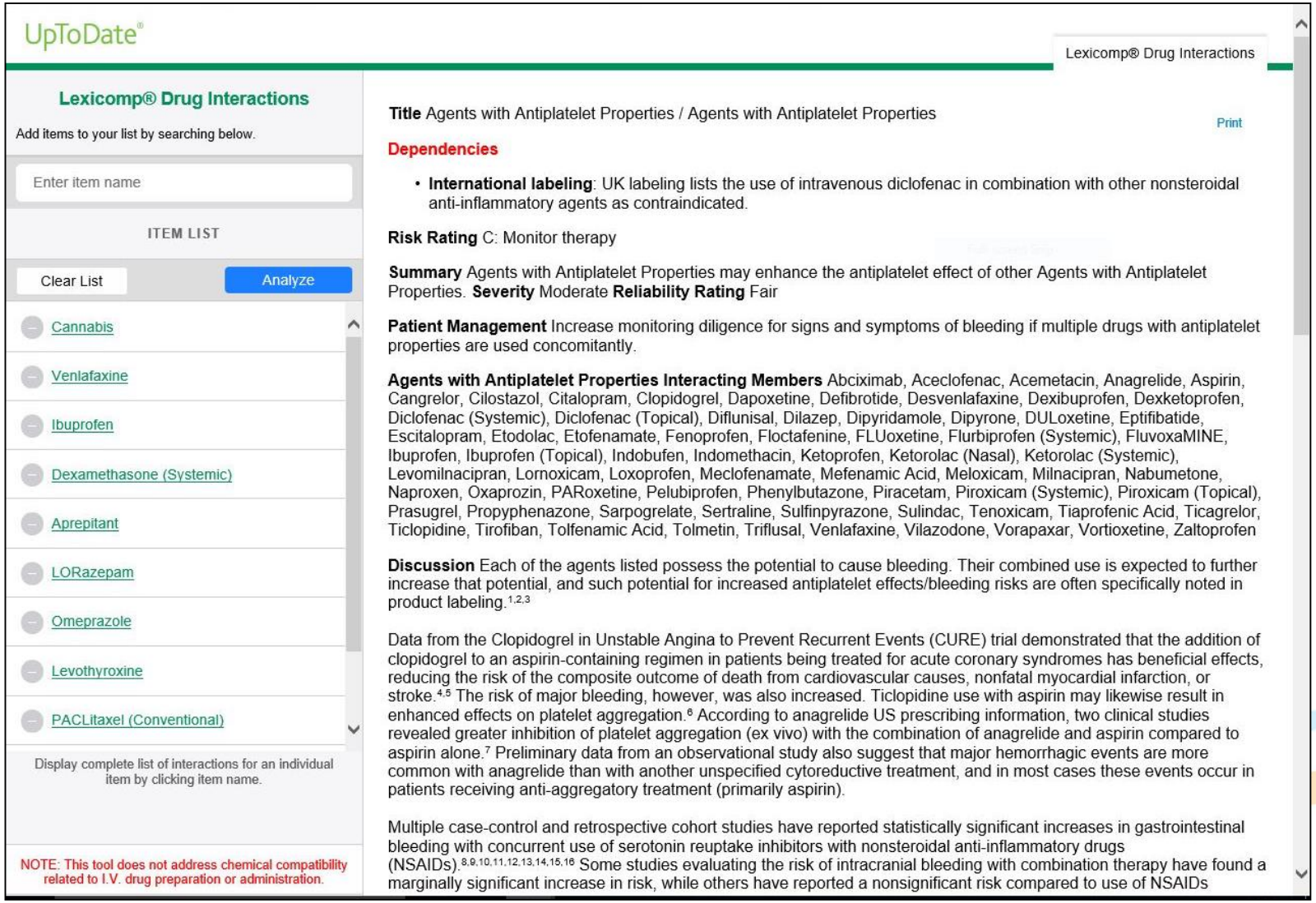
Over-the-counter (OTC) medications NSAIDs



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Over-the-counter (OTC) medications NSAIDs

QUIZ

Non-steroidal anti-inflammatory drugs (NSAIDs)

1. Pain medicines called NSAIDs (non-steroidal anti-inflammatory drugs) are mild painkillers that are safe to take for long periods of time. ◯ TRUE ◯ FALSE
2. NSAIDs do not cause any side effects. ◯ TRUE ◯ FALSE
3. NSAIDs are the best available option to treat my pain symptoms. ◯ TRUE ◯ FALSE
4. Exercise can be effective to reduce pain. ◯ TRUE ◯ FALSE

1. FALSE

It is recommended to take an NSAID at the lowest dose possible for the shortest period of time (1-2 days only).

2. FALSE

NSAIDs are associated with side effects no matter what dose is taken:

- **High blood pressure and heart problems:** If you have high blood pressure, taking medications such as such as NSAIDS could worsen your condition. Make sure you have your blood pressure checked when you start this medication. Using some of these drugs can also cause or exacerbate heart problems or heart failure symptoms because they cause water retention, high blood pressure and more workload for the heart.
- **Stomach ulcers or bleeding:** In patients aged 65 and older, it is suggested to take a stomach protection agent when using an NSAID.
- **Swelling of the ankles:** This symptom can occur from NSAIDs due to water retention.

3. FALSE

Although it may be safe to take NSAIDs over the short term (less than 1-2 days) for some patients, it is generally recommended to use acetominophen or Tylenol®, or use alternative non-medicinal pain treatments such as heat, massage or relaxation when needed.

4. TRUE

Staying physically active can help you manage your pain without taking drugs. Some milder techniques, such as yoga or tai chi, can also help with pain. Discuss your options with your physician.

http://www.criugm.qc.ca/fichier/pdf/Empower_NSAIDS_EN.pdf

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Over-the-counter (OTC) medications Pain

Pain

- Cannabis is now an “OTC” option
- RxFiles 2018 Cannabinoids comparison chart states: “**A note on drug interactions**: Interactions are not fully understood; many are theoretical. Cannabis has many compounds besides THC & CBD; these may have unknown drug interactions. Watch closely for **pharmacodynamic** (additive) interactions.”
- Question: Is it time to be routinely looking for interactions with cannabis and giving the patient personal advise?
  - DrugBank https://www.drugbank.ca/drugs/DB14009
  - Lexicomp Drug Interactions in UpToDate

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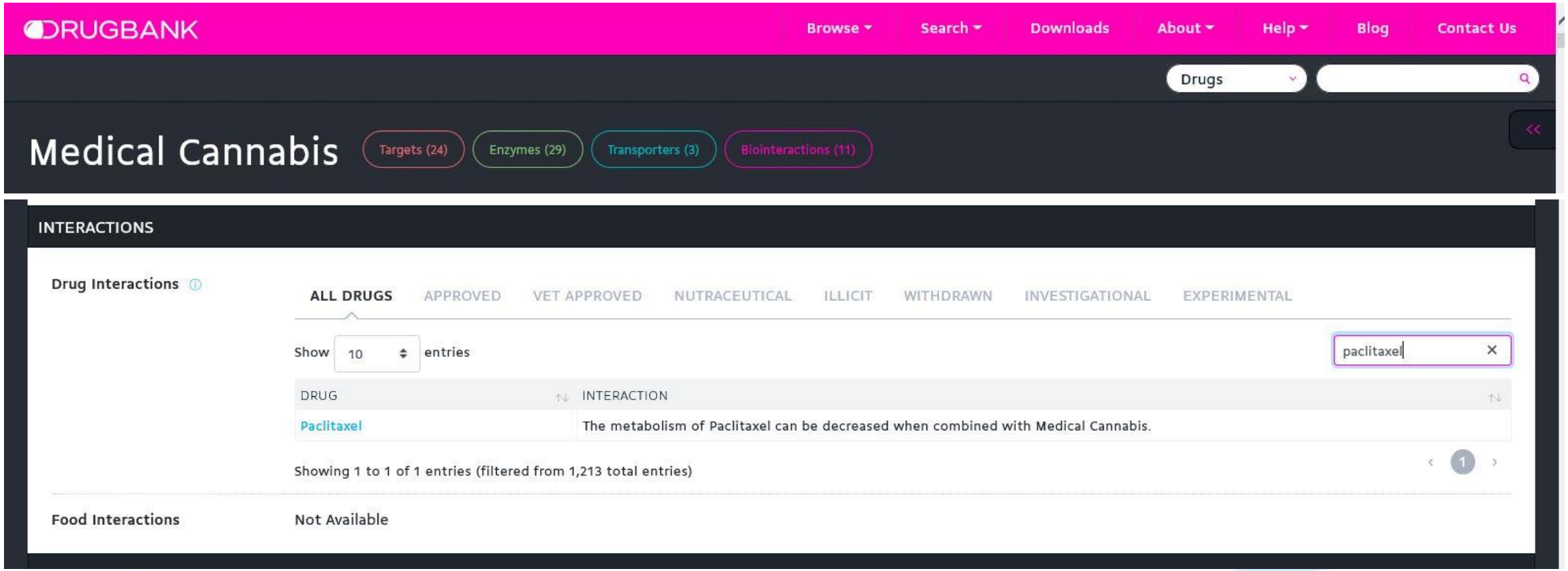
Over-the-counter (OTC) medications Pain



- Every medication Mrs. R is on said “can” be impacted by or impact cannabis

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Over-the-counter (OTC) medications Pain

15 Results

D	Dexamethasone (Systemic) (Corticosteroids (Systemic)) Aprepitant
D	PACLitaxel (Conventional) (Taxane Derivatives) CARBOplatin (Platinum Derivatives)
C	Cannabis Aprepitant (CYP3A4 Inhibitors (Moderate))
C	Ibuprofen (Agents with Antiplatelet Properties) Venlafaxine XR (CAN) (Agents with Antiplatelet Properties)
C	Ibuprofen (Nonsteroidal Anti-Inflammatory Agents (Nonselective)) Dexamethasone (Systemic) (Corticosteroids (Systemic))
C	Ibuprofen (Nonsteroidal Anti-Inflammatory Agents (Nonselective)) Venlafaxine XR (CAN) (Serotonin/Norepinephrine Reuptake Inhibitors)
C	Ibuprofen (Nonsteroidal Anti-Inflammatory Agents) Perindopril and Indapamide (Angiotensin-Converting Enzyme Inhibitors)
C	Ibuprofen (Nonsteroidal Anti-Inflammatory Agents) Perindopril and Indapamide (Thiazide and Thiazide-Like Diuretics)
C	LORazepam (CNS Depressants) Cannabis
C	PACLitaxel (Conventional) (CYP3A4 Substrates (High risk with Inhibitors)) Aprepitant
C	PACLitaxel (Conventional) (Hypotension-Associated Agents) Perindopril and Indapamide (Blood Pressure Lowering Agents)
C	Perindopril and Indapamide (Thiazide and Thiazide-Like Diuretics) Dexamethasone (Systemic) (Corticosteroids (Systemic))
C	Venlafaxine XR (CAN) (CYP3A4 Substrates (High risk with Inhibitors)) Aprepitant
B	Levothyroxine (Thyroid Products) Omeprazole (Proton Pump Inhibitors)
B	Venlafaxine XR (CAN) (Venlafaxine) Omeprazole

UpToDate®

Lexicomp® Drug Interactions

Lexicomp® Drug Interactions

Add items to your list by searching below.

Enter item name

ITEM LIST

Clear List | Analyze

- Cannabis
- Venlafaxine
- Ibuprofen
- Dexamethasone (Systemic)
- Aprepitant
- LORazepam
- Omeprazole
- Levothyroxine
- PACLitaxel (Conventional)

Display complete list of interactions for an individual item by clicking item name.

NOTE: This tool does not address chemical compatibility

Title Cannabis / CYP3A4 Inhibitors (Moderate)

Print

Dependencies

- **Dose**: This interaction is mainly expected when physiologically significant amounts of tetrahydrocannabinol (THC, the major known psychoactive component of cannabis) are introduced systemically. While this encompasses the vast majority of medical and recreational cannabis use, some cannabis strains, products, and routes of administration specifically (and often intentionally) minimize systemic THC exposure. While cannabidiol concentrations are also likely increased by CYP3A4 inhibition, the clinical significance of this increase is less clear.

Risk Rating C: Monitor therapy

Summary CYP3A4 Inhibitors (Moderate) may increase the serum concentration of Cannabis. More specifically, tetrahydrocannabinol and cannabidiol serum concentrations may be increased. **Severity** Moderate **Reliability Rating** Fair

Patient Management Monitor patients who use cannabis in combination with moderate CYP3A4 inhibitors closely for enhanced effects of tetrahydrocannabinol (THC; e.g., cognitive effects, sedation, dizziness, tachycardia) and cannabidiol (CBD; e.g., muscle relaxant effects). No significant interaction has been described, or is expected, between moderate CYP3A4 inhibitors and cannabis strains/products/uses that do not introduce substantial systemic THC or CBD concentrations.

CYP3A4 Inhibitors (Moderate) Interacting Members Aprepitant, Conivaptan, Crizotinib, DilTIAZem, Dronedarone, Duvelisib, Erythromycin (Systemic), Fluconazole, Fosamprenavir, Fosnetupitant, Grapefruit Juice, Imatinib, Isavuconazonium Sulfate, Letermovir, Netupitant, Nilotinib, Ribociclib, Schisandra, Verapamil

Discussion In a clinical study summarized in the U.K. summary of product characteristics for tetrahydrocannabinol (THC) and cannabidiol (CBD) oromucosal spray, coadministration of ketoconazole increased the maximum concentration (Cmax) and AUC of THC by 1.2 and 1.8 fold, respectively, while the Cmax and AUC of its primary hydroxylated metabolite increased by 3 and 3.6 fold, respectively.[1] The Cmax and AUC of CBD both increased by 2 fold.

The suspected primary mechanism of this interaction is ketoconazole inhibition of CYP3A4 mediated metabolism of THC and CBD. Systemic exposure to these cannabinoids administered via other routes (e.g., oral, inhaled) is also expected to increase with coadministration of a CYP3A4 inhibitor. Cannabinol (another cannabinoid commonly found in cannabis and cannabis products) may also be metabolized by CYP3A4, although the significance of this to the clinical effects of cannabis has not been investigated.[2]

Footnotes

1. *Sativex* (tetrahydrocannabinol and cannabidiol oromucosal spray) [UK summary of product characteristics]. Wiltshire, UK: GW Pharma Ltd; February 2014.

2. Watanabe K, Yamaori S, Funahashi T, Kimura T, Yamamoto I. Cytochrome P450 enzymes involved in the metabolism

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Over-the-counter (OTC) medications Anticholinergic

Common symptoms self-treated with OTC's

- Sleep – diphenhydramine (Benadryl), dimenhydrinate (Gravol)
- Nausea - dimenhydrinate
- Diarrhea – loperamide (Imodium)
- Itch – diphenhydramine, other sedating antihistamines

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Over-the-counter (OTC) medications Anticholinergic

Home / Calculate / Result

Anticholinergic burden results

Recalculate PDF XLS

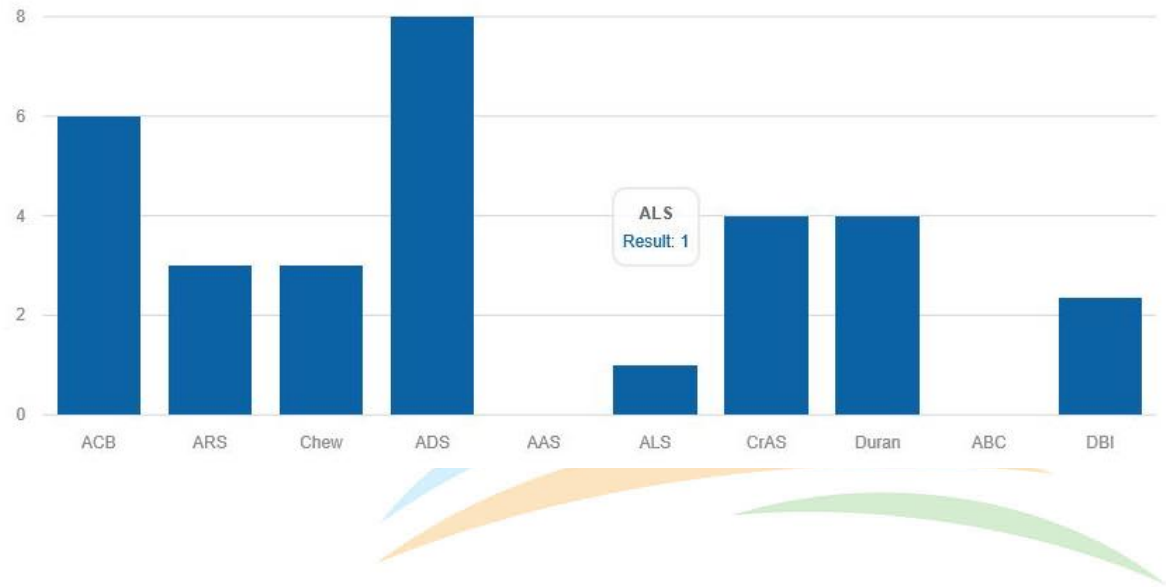
The results of anticholinergic risk (low / medium / high) obtained with each scale are linked to the risk categorization made by the authors or developers of each one of them

Scale	Result	Risk
ACB	6	HIGH RISK
ARS	3	HIGH RISK
Chew	3	MEDIUM RISK
ADS	8	HIGH RISK
AAS	0	WITHOUT RISK
ALS	1	LOW RISK
CrAS	4	HIGH RISK
Duran	4	HIGH RISK
ABC	0	WITHOUT RISK

Medication	Scales								
	ACB	ARS	Chew	ADS	AAS	ALS	CrAS	Duran	ABC
DEXAMETHASONE	0	0	0	1	0	0	0	0	0
DIMENHYDRINATE (50 mg)	3	0	0	3	0	0	0	2	0
DIPHENHYDRAMINE (50 mg)	3	3	3	3	0	0	3	2	0
LORAZEPAM (2 mg)	0	0	0	1	0	0	0	0	0
VENLAFAXINE (150 mg)	0	0	0	0	0	1	1	0	0

DBI Results (Note: This scale, unlike the above, considers drug dose prescribed in the calculation)

Medication	DBI
DEXAMETHASONE	0.00
DIMENHYDRINATE (50 mg)	0.50
DIPHENHYDRAMINE (50 mg)	0.50
LORAZEPAM (2 mg)	0.67
VENLAFAXINE (150 mg)	0.67
Results	HIGH RISK 2.34



http://www.anticholinergicscales.es/

"Web Portal Software Anticholinergic Burden Calculator" is a program designed to measure fast and easily the anticholinergic burden a patient receives based on their pharmacotherapy. "Anticholinergic burden" is defined as the cumulative effect of taking one or more drugs that are capable of developing anticholinergic adverse effects

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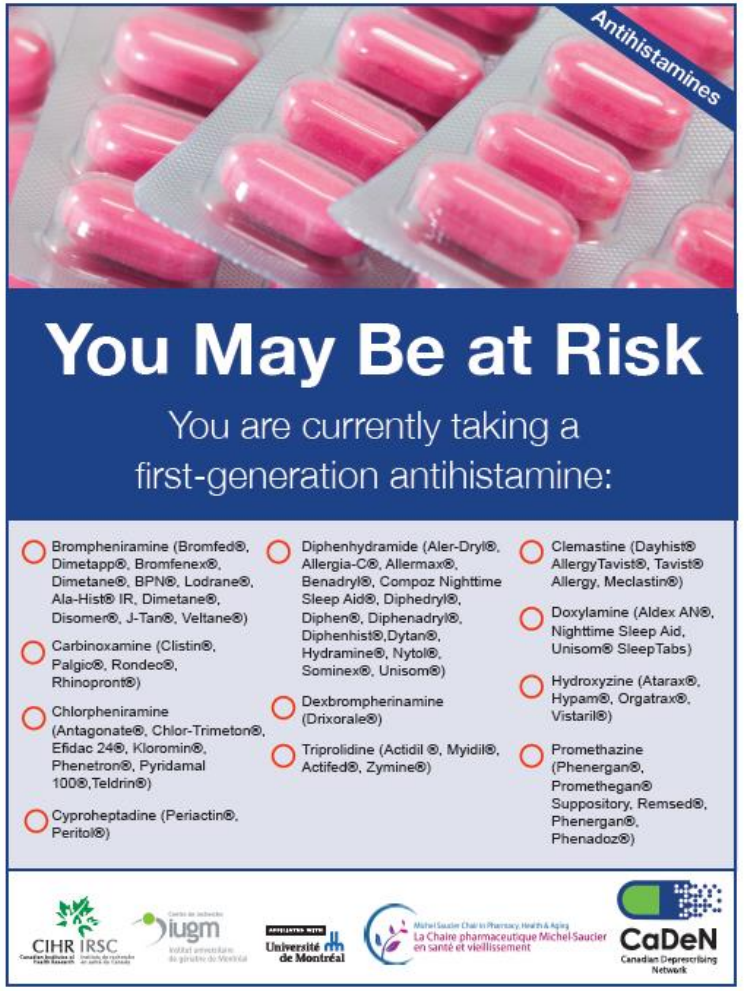
Over-the-counter (OTC) medications Anitcholinergic



DID YOU KNOW?

This medication is a first-generation antihistamine that is used for relief of allergy symptoms such as sneezing, runny nose, sinus and nasal congestion, skin irritations, swelling and itchiness. This medication is commonly known to cause drowsiness. You should therefore never drive or operate heavy machinery while on this drug as it can increase the risk of accidents.

First-generation antihistamines can also cause:

- Dry mouth and dry eyes
- Constipation
- Memory loss, problems with concentration and confusion
- Urinary problems

In some people, this medication can cause a sudden drop in blood pressure leading to dizziness, especially when rising from a chair or bed. People with a history of heart disease, heart failure or glaucoma should use first-generation antihistamines with extreme caution.

WARNING
If you have glaucoma, heart disease or heart failure, you should use medications such as hydroxyzine with caution. You should also avoid taking it at the same time as sleeping pills or with other antihistamines.

Please consult your doctor, nurse or pharmacist before stopping any medication.

http://www.criugm.qc.ca/fichier/pdf/ANTIHISTAMINES.pdf

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Over-the-counter (OTC) medications Delirium

Delirium Prevention and Care with Older Adults

LEARN MORE + PROTECT YOUR BRAIN

Delirium is a medical emergency.

What is Delirium?

Delirium is a sudden and severe disturbance in thinking. It can cause changes in a person's ability to stay alert, remember, be oriented to time or place, speak or reason clearly.

A person with dementia can experience delirium too. Sometimes, delirium can look like dementia. The difference is that delirium comes on quickly. See or talk to a healthcare provider right away if any of the following signs suddenly appear – even if the signs come and go.

- ☐ Having trouble paying attention.
- ☐ Being distracted or unable to follow a conversation.
- ☐ Saying or doing things that do not make sense.
- ☐ Hearing voices or seeing things that other people do not.
- ☐ Developing strange beliefs or thinking people are trying to cause you harm.
- ☐ Being withdrawn, quieter or slower than usual.
- ☐ Being restless, worried, annoyed or angry.
- ☐ Having trouble staying awake during the day and/or not sleeping at night.

Canadian Coalition for Seniors' Mental Health (CCSMH) September, 2016

How is delirium prevented?

To help prevent delirium:

- Make sure those caring for you know all your medications and how you take them. They should be taken as prescribed. Pay extra attention to how you are feeling if you are starting or stopping a medicine or when you are changing how much medicine you take. Talk with your healthcare provider if you are not feeling right.
- Stay physically active.
- Get enough to eat and drink.
- Try to sleep at night (without the help of sleep medicines, if possible).
- Wear your glasses and hearing aids.
- Keep doing hobbies and activities that you enjoy.
- Reduce how much alcohol you drink. Don't stop abruptly.
-

If you are going to the hospital for surgery or other treatment:

- Find out if your hospital has a delirium prevention program. Ask if you can be part of the program.
- Speak to your healthcare team about your risk of delirium after surgery.
- If you experience delirium while in hospital it might be difficult for you to understand your choices for care, make decisions about them and communicate your wishes. Before your surgery or other treatment, let people know what kind of care you would want if you were unable to speak for yourself. See link to *Advance Care Planning* site under *Other Resources* for more information.

https://ccsmh.ca/wp-content/uploads/2017/06/CCSMH-8.5-x-11-Delirium-R1-1.pdf

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Planned deprescribing

Common symptoms

- Sleep
- Anxiety

→ Benzodiazepines and zopiclone

PMH Sedative Deprescribing Initiative supported by the Manitoba Institute for Patient Safety 2018 Dr. John Wade Patient Safety Initiative Grant

- Community arm engaging with hospital pharmacists to plan deprescribing of new sedative benzo’s and z-drugs

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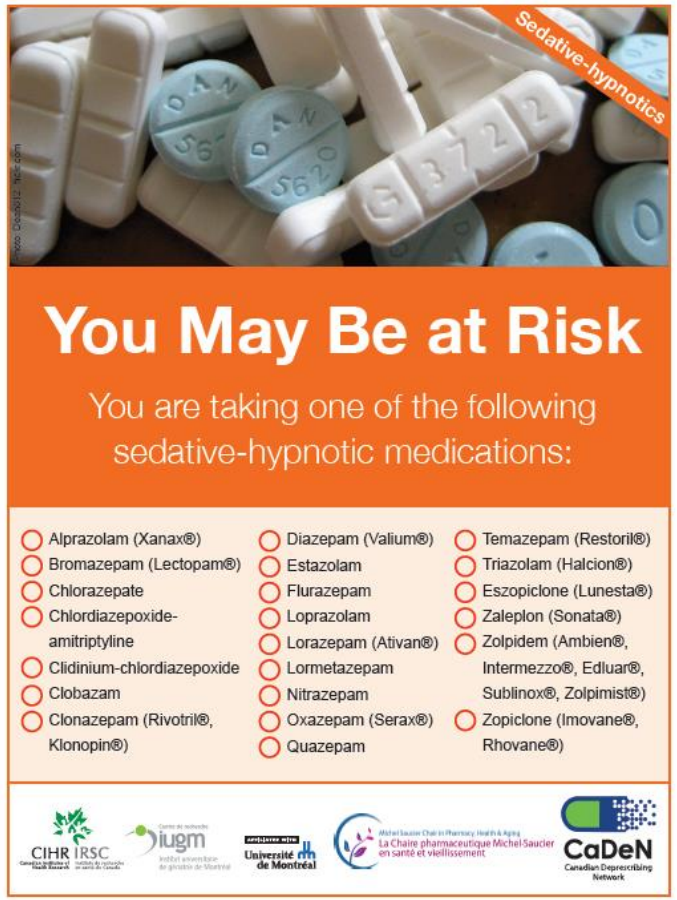
Planned deprescribing



- Since the 1960's people have been told there are safe sleeping pills
  - After a few days to a few weeks nightly use of the medications has no impact on sleep latency or duration of sleep
- The 2018 Benzo' receptor agonist deprescribing clinical practice guideline
  - Strong recommendation for slow taper for people ≥ 65y
- 2014 Cluster Randomized EMPOWER Trial (Tannenbaum et al.) 27% able to discontinue, 11% decreased dose (NNT 3.7)
  - 42% did have some rebound insomnia or anxiety

http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf

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Barriers to Change

- Patient memory for medical information
- Pharmacist resources?
- Review protocols for symptom management that may not be well tolerated as people get older

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Barriers to Change

Patient Memory for Medical Information

- Roy Kessels Journal of the Royal Society of Medicine 2003
- 40 – 80% of medical information provided by providers is forgotten immediately
  - Almost half is incorrect!
- It is easier to learn completely new information than correct previously held beliefs
- Importance of the information impacts recall
  - Diagnosis registers as more important than instructions
- Written information is better remembered

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Barriers to Change

Pharmacist resources?

- Thank you to Kristi Hofer, Senior Pharmacist – Operations CCMB for taking the time to summarize resources
- Always available by phone, some on site services, sometimes part of the clinical team, sometimes doing patient counseling on chemotherapy/anti-cancer treatments
- Winnipeg clinics with NP or FPO do not have onsite pharmacists
- Community Cancer Programs have local hospital pharmacy services

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Barriers to Change

Pharmacist resources?

- Not resourced for medication reviews
- Majority of time is focused on the anti-cancer treatment, oncology expertise
- If interactions warrant a change in home meds the oncologist/hematologist writes a letter to the primary care practitioner
- For primary care type questions retail pharmacists are the primary resource to patients/families/primary care

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Barriers to Change

- Review protocols for symptom management that may not be well tolerated as people get older

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Take home message(s)

- If resources are scarce, the Clinical Frailty Scale (or talk to Dr. Dawe about some of the oncology tools) can help triage people for medication review and counseling about OTCs
  - The correct medication list is the ideal, the current list is a starting point
- Include over-the-counter medications during ongoing review of medications
- In complicated mediation lists look for drug interactions
- Consider the anticholinergic burden and delirium risk

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Question and Answer

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