Adult/Geriatric Drug Therapy 2020

What's New in Geriatrics: An Update on Medications

Carol Crawford, PharmD, BCPS, BCGP

Objectives for Learning Outcomes:

1. Evaluate newly approved medications and their role in therapy for older adults
2. Evaluate new dosing safety updates, including new doses and indications for older medications used in the care of older adults
3. Review current guidelines for disease states associated with the medications discussed today

What's New in Geriatrics: An Update on Medications

Carol Crawford PharmD BCPS BCGP

Newly Approved Medications and Place in Therapy for Older Adults

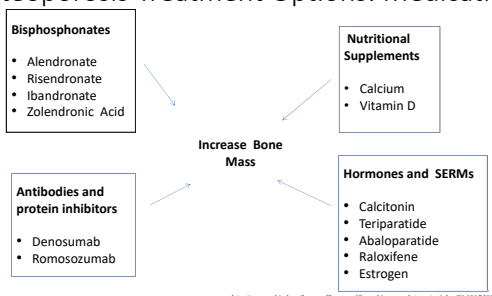
Medication	Brand Name	Indication
Romosozumab	Evenity™	Treatment of Osteoporosis

Evenity™ (romosozumab)

Case:

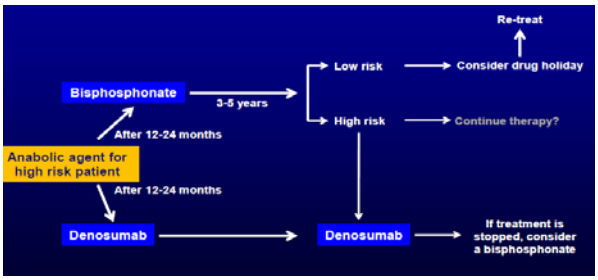
- 76 year old female referred for review/assessment of osteoporosis tx.
- Last DEXA: 2014 Tspine -3.0, T left femur -2.0
- Hx of fx: lumbar fx Apr 2020 2/2 fall. 2014 femur fx (setting of bisphosphonate)
- Labs: SCr:0.51, Ca 10.5, D tot: 45.8 (2018)
- Taking Ca/D supplements: D3 1000iu daily
- Past Medications used: - bilateral subtrochanteric femur fxs (2014) while on bisphosphonate. 2 years teriparatide (2014-2016), Raloxifene 60mg daily (2017-2019) Currently on 1 month of calcitonin nasal spray started 4/17/20
- Medication recommendation once Ortho clears pt to start?

Osteoporosis Treatment Options: Medications



http://www.ncbi.nlm.nih.gov.offcampus.lib.washington.edu/pmc/articles/PMC3758213/figure/f2-ddt-7-849/

Osteoporosis Treatment Plan



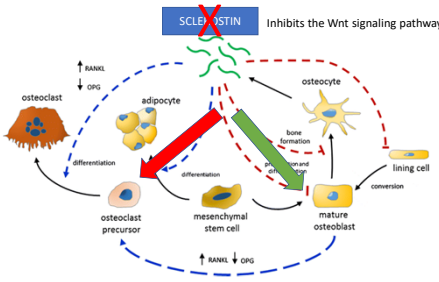
McClung, M. (2018). Current Issues in Osteoporosis. PowerPoint presentation at the California AACE 18th Annual Meeting and Symposium, Marina del Rey, CA

Evenity™ (romosozumab)

- FDA approved for the treatment of osteoporosis in postmenopausal women at high risk of fracture
- MOA: An anti-sclerostin monoclonal antibody
- Sclerostin is made primarily by osteocytes. It inhibits bone formation and enhances apoptosis of osteoblasts
- Inhibiting sclerostin stimulates bone formation and reduce bone resorption, with a robust increase in BMD

Romosozumab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://www.uptodate.com. Accessed Aug 10, 2019

Effects of Sclerostin



Delgado-Calle, J. McDonald MM. Current Osteoporosis Reports. 2017.;Vol 15(6),:532-541

Evenity™ (romosozumab)

Dose:

- 2 consecutive subQ injections (105mg each) for a total dose of 210mg every 4 weeks
- No adjustments for renal or hepatic impairment needed
- Treatment Duration: 12 months
- Bone mineral density (BMD) returns to baseline ~ 12 months after treatment completion

Romosozumab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://www.uptodate.com. Accessed Aug 10, 2019

Warnings, Precautions and Side Effects

BBW: Potential risk of MI, stroke and cardiovascular death

- Atypical fractures or osteonecrosis of the jaw
- Hypocalcemia

Side Effects:

- Neuromuscular and skeletal arthralgias (8-13%)
- Headache (5-7%)
- Hypersensitivity (7%)
- Cardiac disorder (2%), peripheral edema (2%), insomnia (2%)

Romosozumab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://www.uptodate.com. Accessed Aug 10, 2019

Evenity™ (romosozumab)

- Geriatric Use: no specific geriatric dosing
  - Mean age in trials = 71-73 years
- Cost: approx $22,000/year ($935.00/syringe)- similar to abaloperitide

Romosozumab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://www.uptodate.com. Accessed Aug 10, 2019

Anabolic Agent Comparison

- PTH analogs (teriparatide, abaloparatide):
  - Strong evidence: reduction of Vertebral fractures
  - Fair evidence: reduction of Nonvertebral fractures
  - Weak evidence: reduction of Hip fractures
- Previous bisphosphonate treatment attenuates the bone-forming effect of teriparatide

Anabolic Agent Comparison

STRUCTURE

Teriparatide

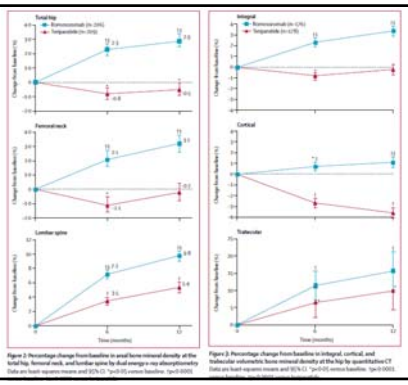
Romosozumab

12 Months

- International RTC - open label
- 436 Females patients ≥ 55 and ≤ 90 yrs with Tscore = ≤ -2.5 at hip, femoral neck, or spine (ave Thip -2.2, Tspine -2.8)
- H/o vertebral or nonvertebral fx at > 50 yrs
- 3 years of bisphosphonate use immediately prior (mean 5.6 yrs use)

Langdahl BL. The Lancet. 2017; 390:1585-1594

Anabolic Agent comparison : STRUCTURE trial



Anabolic Agent comparison : STRUCTURE trial

Primary Endpoint:

- Mean percentage change from baseline in total hip areal BMD:
  - 2·6% (95% CI 2·2 to 3·0) in the romosozumab group and −0·6% (−1·0 to −0·2) in the teriparatide group; difference 3·2% (p<0·0001)
- Adverse events balanced between treatment groups:
  - nasopharyngitis (13%) *vs (*10%) in the teriparatide group)
  - hypercalcemia (<1%) *vs* (10%)
  - arthralgia (10%) *vs* (6%)
  - No CV events, atypical fxs or jaw osteonecrosis reported

Romosozumab increased BMD after bisphosphonate use

Langdahl BL. The Lancet. 2017; 390:1585-1594

Evenity™ (romosozumab) : Place in Therapy

- Post fracture therapy? Pre-clinical trials showed enhanced fracture healing
- Evidence immerging to support beginning with anabolic agent in patients with high or imminent risk of fracture
- BRIDGE trial – 12 m romosozumab vs placebo in men

Evenity™ (romosozumab) : Place in Therapy

- CV adverse events – statistical vs clinically relevant
- Postmenopausal women:
  - ARCH trial-- Romosozumb vs. Alendronate:

    CV events: 2.5% R vs 1.9% A (OR 1.31; 95% CI 0.85-2.0), Cardiac ischemic events: 0.8% R vs 0.3% A (OR 2.65; 95% CI 1.03-6.77)
- FDA requiring post-marketing data to review
- CHMP* (European FDA equivalent) denied approval

*CHMP= Committee for Medicinal Products for Human Use

Arteriosclerosis, Thrombosis, and Vascular Biology. 2019;39:1343–1350

What's New with Old Drugs

Medication	
Apixaban	New dosing for CKD, new reversal agent
Iron	Every other day dosing
Trazodone	Safety compared to benzodiazepines
Cannabis	Efficacy and safety review

Eliquis™ (apixaban): An update

Case:

91 yo female pt of SCC currently on warfarin for afib.

CHA2DS2-VASc Score: 5 (HTN, age(2), DM, CAD)

HAS-BLED Score: 3 (age, h/o GIB, clopidogrel) as of 3/2020

- Relevant historic Information: Switched from apixaban to warfarin due to declining renal function (CrCl consistently <25ml/min). Dtr stating much more bruising with warfarin and more than anticipated INR draws needed . (INRs over last 4 months have occillated between 1.5-5.5). Dtr wishing to restart apixaban.

New dosing recommendations for Apixaban

- **Severe or ESRD not requiring hemodialysis**
- Apixaban or warfarin is considered appropriate. Some experts recommend apixaban 2.5 mg twice daily for CrCl 15 to 29 mL/minute

- **ESRD requiring hemodialysis**
- Not dialyzable to minimally dialyzable (AUC decreased by 14% over 4 hours). According to the manufacturer, no dosage adjustment necessary **unless** either ≥80 years of age or body weight ≤60 kg, then reduce to 2.5 mg twice daily.

Manning WJ. Management of thromboembolic risk in patients with atrial fibrillation and chronic kidney disease. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed May 2, 2020.

New dosing recommendations for Apixaban

- **2019 AHA/ACC/HRS Focused Update on Guideline for the Management of Patients With Atrial Fibrillation:**

- For pts with CHA2DS2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage chronic kidney disease (CrCl <15 mL/min) or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0 to 3.0) or apixaban for oral anticoagulation

January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS guideline for the management of patients

DOACs vs Warfarin : Summary

- Trending that DOACs are just as effective or better than warfarin for AF and VTE
  - BUT **absolute difference is minimal**
- Safety outcomes
  - Mostly no difference in major bleeding
  - Slight differences between DOACs vs warfarin in regards to GIB, hemoglobin level drop, need for transfusion

N Engl J Med. 2013;369(9):799-808.
N Engl J Med. 2013;369(9):2499-510.
N Engl J Med. 2013;369(9):1406-15.
Circulation.2014;129(7):764-72.

Apixaban for Patients ≥ 75 years

Sharma et al. (2015)	Meta-analysis with 11 studies compared to warfarin
Primary efficacy outcomes (stroke or systemic embolism, recurrent VTE)	AF studies: Reduction in risk (OR 0.70; 95% CI, 0.52-0.93; p=0.01) VTE studies: Non inferior to warfarin
Primary safety outcome (major bleeding)	Reduction in risk (OR 0.63, 95% CI 0.51-0.77; p<0.0001)
ICH	Reduction in Risk (OR 0.38, 95% CI 0.24-0.59 p<0.0001)
Other bleeds (fatal)	No significant difference

Major bleeding : any bleeding requiring hospitalization, causing a decrease in hemoglobin level > 2 g/L, requiring blood transfusion. Excludes hemorrhagic stroke.

Circulation.2015; 132(3):194-204.

Apixaban: Dosing

Nonvalvular AF	VTE Prophylaxis	VTE Treatment
5mg BID OR 2.5mg BID If patient has any 2 of the following: Age ≥ 80 years Weight ≤ 60kg Scr≥ 1.5 ml/dL	2.5mg BID 12-24 hours post-op	10mg BID x 7 days Then 5mg BID Switch to 2.5mg BID for long term prevention after 6 months of treatment *
Patients with SCr>2.5 mg/dL or CrCl< 25ml/min were excluded from NVAF trials Patients with CrCl< 15ml/min and ESRD on dialysis excluded from VTE trials 2.5mg dose administered to only 5% of patients in NVAF trials		

Apixaban. Lexi-Drugs. Lexicomp. Walters Kluwer Heath, Inc. Riverwoods, IL. Available at :http://www.uptodate.com. Accessed July 1, 2019. N Engl J Med 2011; 365:981-992. *www.micromedexsolutions.com. Accessed May 1, 2020

Apixaban: Safety in CKD

- No RTCs for pts with creatinine clearance < 15 mL/min, or undergoing dialysis– ACC/AHA AF guidelines recommend warfarin (IIa/ level B rec)
  - RENAL-AF and AXA-DIA (RTCs of Afib pts on apixaban vs warfarin in ESRD on dialysis) ongoing

- Least renally dependent DOAC (~25% renal elimination)

https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product information_en.pdf

Warfarin Safer in CKD?

Retrospective Study (apixaban vs warfarin for NVAF and VTE)

– 604 pts CKD4, 5 and and CKD 5 on dialysis- median age 74 yrs

Primary End pt : major bleed (months)	Apixaban vs Warfarin
0 to 3 months	8.3% vs 9.9% (P= 0.48)
3 to 6 months	1.4% vs 4% (P=0.07)
6-12 months	1.5% vs 8.4% (P<0.001)

- More females and older, more h/o bleeds in the apixaban group
- Comparable rate for secondary end pt of ischemic stroke and VTE rates

Schafer JH, Casey AL, Dupre KA et al. Safety and Efficacy of Apixaban Versus Warfarin in Patients With Advanced Chronic Kidney Disease. Ann Pharmacother. 2018; 52(11) 1078-1084

Warfarin Safer in CKD 5 on Dialysis?

Retrospective cohort study (apixaban vs warfarin for NVAF)

– 25,523 pts with CKD 5 on dialysis- mean age 68.2 yrs, 45 % women (matched ratio 1:3)

5mg BID apixaban vs warfarin:

- Sign lower risk for : Stroke/SE (HR 0.64)
  Major Bleed (HR 0.72)

5mg BID apixaban vs 2.5mg BID:

- Sign lower risk for: Stroke/SE: (HR 0.61)

2.5mg BID apixaban vs warfarin:

- Sign lower risk for: Major Bleed (HR 0.64)

Sionis KC, Zhang X, Eckard A, et al. Outcomes Associated with Apixaban Use in End-Stage Kidney Disease Patients Wth Atrial Fibrillation in the United States. Circulation. 2018;138:1519–1529

Apixaban: To measure or not to measure

- DOAC level measurement needed: Inpatient acute/chronic renal insufficiency; significant bleeding, recurrent VTE/therapeutic failure, urgent surgery/invasive procedures
- Potentially useful : body weight, presence of interacting medications, and confirmation of chronic anticoagulation following initial loading period

- **Apixiban Assay (APIYN1)--Calibrated quantitative anti-Factor Xa assay**
  - Anti-FXa activity exhibits a linear relationship with apixaban plasma concentration
  - Results are available between 1 (stat) and 4 hours (routine)

- Lower limit of measurable range is < 20 ng/ml .
- Trough provides steady state, correlated to bleed rate
- No therapeutic range has been determined

https://www.clinicalcorrelations.org/2019/04/09/is-there-a-role-for-doac-level-monitoring-in-clinical-practice/
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Product_Information/human/002148/WC500107728.pdf

Apixaban: To measure or not to measure

Apixaban dose	Observed Peak Concentration	Observed Trough Concentration
VTE Prophylaxis		
2.5mg bid	41-146 ng/ml	23-109 ng/ml
VTE Treatment		
2.5mg bid	30-153 ng/ml	11-90 ng/ml
5mg bid	69-302 ng/ml	22-177 ng/ml
10mg bid	111-572 ng/ml	41-335 ng/ml
Stroke Prevention in AF		
2.5mg bid	69-221 ng/ml	34-162 ng/ml
5mg bid	91-321 ng/ml	41-230 ng/ml

https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf

Reversal Agent: AndexXa™ (andexanet alpha)

- FDA approved for the reversal of rivaroxaban and apixaban when reversal is needed due to life-threatening or uncontrolled bleeding

- MOA: recombinant coagulation factor Xa (FXa) that binds and sequesters the Fxa inhibitors. Also inhibits the activity of tissue factor pathway inhibitor, increasing tissue factor-initiated thrombin generation

AndexXa [package insert]. Portola Pharmaceuticals: 12/2018

AndexXa™ (andexanet alfa)

- Low dose: 400mg IV (30mg/min), followed by IV infusion of 4 mg/min
- High dose: 800 mg IV (30mg/min), followed by IV infusion of 8mg/min

Andexanet Alfa Dose Based on Apixaban or Rivaroxaban Dose[a]			
Factor Xa inhibitor	Factor Xa inhibitor last dose	Timing of factor Xa inhibitor last dose before andexanet alfa initiation	
		<8 Hours or Unknown	≥8 hours
Apixaban	≤5 mg	Low dose	Low dose
	>5 mg or unknown	High dose	
Rivaroxaban	≤10 mg	Low dose	
	>10 mg or unknown	High dose	

AndexXa [package insert]. Portola Pharmaceuticals: 12/2018

AndexXa™ (andexanet alfa)

- **Side Effects/Warnings:**
  - Infusion-related rxn (18%), antibody development (6-17%)
  - DVT (6%), ischemic stroke (5%), acute MI (3%), PE (3%)
  - Urinary tract infection (≥5%), pneumonia (≥5%)
- **Geriatric use:** No geriatric specific dosing
  - Mean age in clinical trials = 77 years
- **Cost:** $26,400 (low dose), $52,800 (high dose)

Not on UW formulary: AndexXa ™ will likely correct anti-Xa values, but the correlation of lab results with improved clinical outcomes has not been established

AndexXa [package insert]. Portola Pharmaceuticals: 12/2018

KEY TAKEAWAYS

Retrospective studies support apixaban use in advanced CKD and ESRD on dialysis from a safety and efficacy prospective in NVAF
- Appears safer than warfarin from a bleed standpoint
- Dosage still a little unclear

FDA approved reversal agent increases the safety profile for apixaban (unclear cost vs benefit)

Xa monitoring intended only to confirm apixaban activity vs guide dosing

Every other day dosing of Iron

Take- Home Message

Iron absorption is improved with alternate daily dosing vs. daily dosing

Current Treatment Recommendations by AFP for Iron Deficiency Anemia

Form	Elemental Iron	Adult Dosage
Ferrous fumarate 324 mg tablet	106 mg	1 tab BID
Ferrous gluconate 300 mg tablet	38 mg	1-3 tabs BID or TID
Ferrous sulfate 325 mg tablet	65 mg	1 tab TID

AFP= American Family Physicians

https://www.aafp.org/afp/2013/0115/p98.html

Barriers

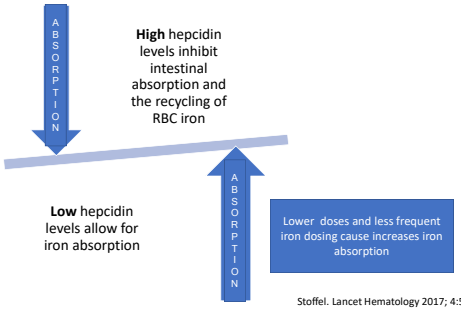
- Adherence due to adverse effects (nausea, diarrhea, constipation, upset stomach)
- Taking with food can help but absorption can decrease by 40%

Evidence: Dosing Studies

- Once daily vs BID dosing
  - 120mg $FeSO_4$ at 8AM vs 60mg $FeSO_4$ at 8AM and 5PM
  - No significant difference found in fractional or total iron absorption
- Once daily vs Alternate day dosing
  - 60mg $FeSO_4$ daily x 14 days → Total iron absorption: 131mg
  - 60mg $FeSO_4$ QOD x 28 days → Total iron absorption: 175.3mg

Stoffel. Lancet Hematology 2017; 4:524-33

Proposed Mechanisms: Hepcidin a key regulator of iron balance



Stoffel. Lancet Hematology 2017; 4:524-33

KEY TAKEAWAYS

NO BENEFIT IN DIVIDED DAILY DOSES
When doses were split into BID there was no difference in iron absorption vs once daily dosing

BETTER ABSORPTION WITH ALTERNATE DAILY DOSING
Iron absorption was improved with alternate daily dosing due to the paradoxical increase in hepcidin with once daily dosing

IMPROVED TOLERABILITY
33% less nausea and abdominal pain with alternate daily dosing= greater potential adherence

Trazodone for Insomnia

Take-Home Message

Low dose trazodone is no safer than new use of benzodiazepines for avoiding fall-related injuries and hospitalization in nursing home residents.

Low-Dose Trazodone, Benzodiazepines, and Fall-Related Injuries in Nursing Homes (NH): A Matched-Cohort Study

- 5 yrs – All NHs in Ontario, Mean age = 84 yrs
- Propensity score matching to avoid bias d/t confounding
- Median trazodone dose = 50mg (25mg-107mg)
- Median lorazepam dose = 1.0mg (0.75mg-2.1mg)
- 40% pts on concurrent antipsychotics/antidepressants/cholinesterase inh
- Results may have been underestimated by focusing on ED/hospitalization

Evidence: Matched Cohort Study

Analysis	Trazo	Benzo	HR (95% CI)	P-value
Primary: Fall-related ED or Hosp w/in 90 days	5.74%	6.03%	0.95 (0.83-1.08)	0.43
Secondary: Hip or wrist fx dx ED visit or Hosp w/in 90 days	1.22%	1.54%	0.79 (0.60-1.04)	0.09

No cohort safer (sex, fragility, dementia)

Bronskill SE, et al. JAGS, 2018

Cumulative Incidence for Fall-related Injuries

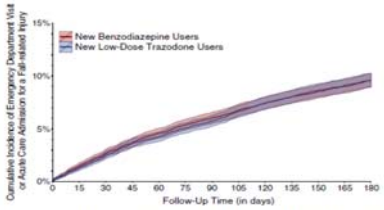


Figure 2. Cumulative incidence functions for fall-related injuries in Ontario nursing homes residents dispensed low-dose trazodone benzodiazepines between April 1, 2010, and March 31, 2015.

Bronskill SE, et al. JAGS, 2018

Cannabis use in the Elderly

Take – Home Message

Risk very likely outweighs vague benefit of cannabinoid use in the elderly

Cannabis

81 yo pt with neuropathic pain 2/2 to DM2 and spinal osteoarthritis. Pregabalin 75mg BID and duloxetine 60mg daily not helping sufficiently.

Son bought pt some cannabidiol (CBD) oil to trial. Pt states that CBD oil is safe because it doesn't make you high.

Are our patients actually using this stuff?

Yes!

From 2006-2013, the prevalence of past-year cannabis use among adults aged ≥ 65 had a relative increase of:

A. 50%
B. 100%
C. 150%
D. 200%
E. 250%

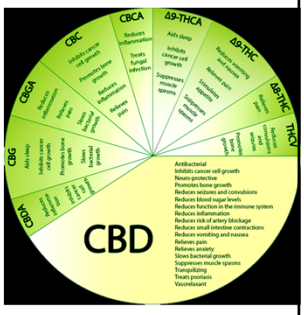
Benjamin Han. Addiction. 2017 March ; 112(3): 516–525. doi:10.1111/add.13670.

Why are seniors turning to cannabis?

- Aches and pains that are difficult to treat/relieve
- Other symptoms that are difficult to treat (PTSD, anxiety, insomnia, depression, weight loss)
- Over the counter! And legal now!
- Baby Boomers may have tried it before
- It's "natural" and therefore must be "safe"
- It's not "addictive" like opioids
- Their kids gave it to them to try
- Marketing and Field Trips (it is a business after all)

Cannabis Terminology

- Cannabis sativa – actual scientific name of the plant
- (Phyto)Cannabinoids- unique chemical structures found in the cannabis plant which includes:
- CBD (cannabidiol)
- THC (tetrahydrocannabinol)
- THCA (tetracannabinolic Acid) –Δ9-THC most common and bred for recreational use



https://carebydoctors.com/what-is-cbd/

Cannabis Pharmacology

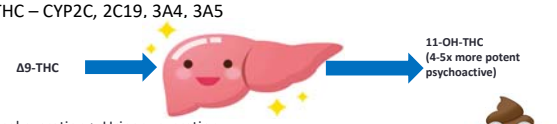
Route	Time to effect	Duration
Oral/Sublingual (edibles, tinctures, sprays)*	30min-4 hours	6-8 hours
Inhaled (Combustion, Vaporization)	Within minutes	A few hours
Topical/Transdermal	Within minutes	~2-3 hours depending on base
Rectal/Vaginal (Yes, suppositories are available)	???	???

*Increased absorption with food/fed state, lipophilic, doses often a very small portion of the sold product

National Academies of Sciences, Engineering, and Medicine. 2007

Metabolism

- Extensive hepatic metabolism! (= extensive drug interactions), diff effects on diff CYP450 isoforms
- CBD – CYP3A4, 2C19, 2D6, 2E1, 3A4, 3A5
- THC – CYP2C, 2C19, 3A4, 3A5



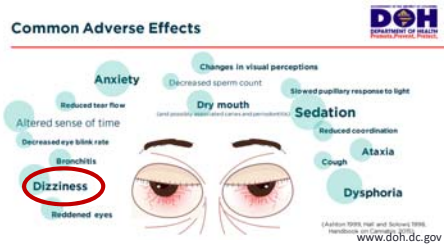
- Fecal excretion > Urinary excretion
- Clearance minimally changed in renal failure

Drug Interactions

- Warfarin! (↑INR)
- Anticholinergics (additive, eg ↑ sedation)
- Benzodiazepenes/Barbiturates (additive CNS depressant)
- Alcohol (may ↑THC levels)
- CBD may increase levels of SSRIs, TCAs, antipsychotics, Beta blockers, opioids, certain NSAIDs and antivirals, PPIs

Seamon 2007, Aggarwal 2013

Side Effects, Risks, Harm



www.doh.dc.gov

Medical Harm Concerns

- **Cardiovascular**: Cannabis likely ↑s heart rate, supine BP and (in higher doses) postural hypotension
  - Insufficient evidence of CV harm in short or long term light use
  - Recall bias, no data about longitudinal exposure
- **Pulmonary Function**: Cannabis may be associated w/ ↑symptoms of cough, sputum production, and wheezing
  - Moderate strength evidence that no AEs for low levels of smoking among **young** adults
  - Little data on heavy use or in older chronically ill patients
- **Cancer (Lung, Head and Neck):**
  - Low strength evidence for no association

Mental Health Harm Concerns

- All in young people
  - Suicidal Behaviors: Insufficient evidence
  - Mania: Possible dose-response ↑ new-onset mania
  - Cognitive Effects: Moderate strength evidence that long-term use assoc w/ small negative effects on all domains of cognition
  - Psychosis: Low strength evidence that hx of cannabis use assoc w/ ↑risk of developing psychotic symptoms
- No studies in CBD alone or CBD dominant products

FDA approved medications

	Dronabinol	Nabilone	Cannabidiol	Nabiximols
Brand Name	Marinol	Cesamet	Epidiolex	Sativex
What is it?	**Synthetic Δ9-THC** (equal affinity for CB1 and 2, but less efficacy at CB2)	**Synthetic THC analog** (cannabinoid binds CB1 and CB2)	**Purified CBD** from cannabis plant	**1:1 THC to CBD** mixture (extract)
Route	Capsule	Capsule	Oral Solution	Oromucosal Spray
Indication	Chemotherapy related N/V, appetite stimulant in AIDS pts	Chemotherapy related N/V	Refractory seizures in Dravets and Lennox-Gastaut Sx (>2yo)	Symptomatic relief of muscle spasms
Onset	30-60min	60-90min	2.5-5hrs	30-150min
Duration	4-6hrs	8-12hrs	Half life 56-61hrs	Variable

Four areas identified as offering evidence regarding effectiveness of cannabis or cannabinoids:
- Antiemetic for chemotherapy-induced nausea and vomiting (cannabinoids)
- Multiple Sclerosis spasticity symptoms (cannabinoids)
- Chronic pain (cannabis)
- Refractory seizures (cannabinoids)

National Academies of Sciences, Engineering, and Medicine 2017)

Advice for Geriatricians

- Open up the conversation
- Ask pts specifically if they are using cannabis, or even considering it (especially if they have symptoms that have been challenging to manage)
- Ask caregivers (like adult children)
- Share that you are open and willing to discuss how cannabis might fit into their medical care
- Do not discuss all risks upfront; appearing too negative immediately may push pts to assume you will judge them for considering and/or using cannabis
- Align by using "I hope" statements, avoid "but"s

KEY TAKEAWAYS

SCANT EVIDENCE TO SUPPORT CANNABIS USE AMONG OLDER ADULTS:

Largely unknown risk-benefit ratio in a high risk, vulnerable population

If prescribing/counseling :

- Use high cannabidiol (CBD) to tetrahydrocannabinol (THC) ratio to limit the psychoactive effects of marijuana
- Consider topicals to reduce systemic absorption
- Screen for potential DDIs/Drug-disease state interactions

Be prepared to initiate open conversations about cannabis use to stay ahead of the direct to consumer market

Thank You

Carol Crawford PharmD BCPS BCGP