Clinical Pearls for the Practicing Pharmacist

MPhA – April 18, 2024

Richard L. Ogletree, Jr., PharmD
bogletree3@gmail.com

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Financial Disclosures and C.E. Information

Dr. Ogletree declares that he has the following affiliations with ineligible companies related to the subject matter of this continuing pharmacy education activity:

Telligen – pharmacy director

Advanced Infusion Systems – research coordinator

MPhA and DPPD have taken additional steps to mitigate this potential conflict of interest by restricting discussion of certain topics.

The University of Mississippi School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.
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Activity type: knowledge
Credits: 1 hour (0.1 CEU)

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Learning Objectives

At the end of this program, the participant will be able to:

- Identify potential opportunities for clinical pharmacy activities
- Recognize medications appropriate for titration
- Recall FDA alerts involving commonly used medications
- Recall medications appropriate for heat precautions

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Community and/or distributive pharmacists commonly have the opportunity to practice clinical pharmacy.

A. True
B. False

4

Abridged Definition - ACCP

- The area of pharmacy concerned with the science and practice of rational medication use.

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Unabridged Definition

Clinical Pharmacy is a health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention. The practice of clinical pharmacy embraces the philosophy of pharmaceutical care; it blends a caring orientation with specialized therapeutic knowledge, experience, and judgment for the purpose of ensuring optimal patient outcomes. As a discipline, clinical pharmacy also has an obligation to contribute to the generation of new knowledge that advances health and quality of life.

Clinical pharmacists care for patients in all health care settings. They possess in-depth knowledge of medications that is integrated with a foundational understanding of the biomedical, pharmaceutical, socio-behavioral, and clinical sciences. To achieve desired therapeutic goals, the clinical pharmacist applies evidence-based therapeutic guidelines, evolving sciences, emerging technologies, and relevant legal, ethical, social, cultural, economic and professional principles. Accordingly, clinical pharmacists assume responsibility and accountability for managing medication therapy in direct patient care settings, whether practicing independently or in consultation/collaboration with other health care professionals. Clinical pharmacist researchers generate, disseminate, and apply new knowledge that contributes to improved health and quality of life.

Within the system of health care, clinical pharmacists are experts in the therapeutic use of medications. They routinely provide medication therapy evaluations and recommendations to patients and health care professionals. Clinical pharmacists are a primary source of scientifically valid information and advice regarding the safe, appropriate, and cost-effective use of medications.

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Important Points

Clinical pharmacists:

- care for patients in all health care settings
- are experts in the therapeutic use of medications
- are a primary source of scientifically valid information and advice regarding the safe, appropriate, and cost-effective use of medications

7

Titrating Medications

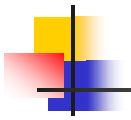
- Why?
  - Narrow therapeutic window
  - Patient response variability
  - Avoid adverse effects/events
  - Achieve maximum benefit with lowest dose

8

What is the starting dose of doxazosin (Cardura®) /terazosin (Hytrin®)?

A. 1 mg
B. 2 mg
C. 4 mg/5 mg
D. 8 mg/10 mg

9



Doxazosin

- The initial dosage of doxazosin mesylate is 1 mg, given once daily in the a.m. or p.m.
- The recommended titration interval is 1 to 2 weeks to 2 mg and thereafter to 4 mg and 8 mg once daily, the maximum recommended dose for BPH.

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Doxazosin

Marked orthostatic effects are most common with the first dose but can also occur when there is a dosage increase, or if therapy is interrupted for more than a few days.

11

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12

Gabapentin

Side effects common with initiation

- fatigue
- somnolence
- drowsiness

13

Gabapentin

- The starting dose is 300 mg three times a day
- The dose may be increased using 300 or 400 mg capsules three times a day up to 1800 mg/day. Doses of 2400-3600 mg/day have been utilized.

14

Lamotrigine (Lamictal®)

- The initial dosage of lamotrigine is 25 mg every day.
- The recommended titration schedule is 25 mg/day for weeks 1 and 2, 50 mg/day weeks 3 and 4, increase by 50 mg/day every 1 to 2 weeks to a maintenance dose

15

Lamotrigine (Lamictal®)

Black Box Warning includes "There are suggestions, yet to be proven, that the risk of rash may also be increased by

- coadministration of LAMICTAL with valproate
- exceeding the recommended initial dose of LAMICTAL
- exceeding the recommended dose escalation for LAMICTAL

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Concomitant Medications

- Valproate- need smaller doses
- Carbamazepine, Phenytoin, Phenobarbital, or Primidone- need larger doses

17

Mixed Amphetamine Salts

- Start with 5 mg once or twice daily
- Daily dosage may be raised in increments of 5 mg at weekly intervals until optimal response is obtained
- MAX
  - 40 mg/day ADD
  - 60 mg/day Narcolepsy
  - Good Luck
  - Use PMP

18

Levothyroxine

- Very commonly used
- Hypothyroidism
  - primary
  - secondary
- Weight loss - not a good idea

19

Levothyroxine

- Increased heart rate and possible angina symptoms in cardiac patients
- Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects

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Levothyroxine Prescribing information

- In otherwise healthy adults less than 50 years of age and in those over age 50 years recently treated for hyperthyroidism or hypothyroid for only a few months, therapy may begin at full replacement doses (100 to 125 mcg/day for a 70 kg adult)
- Over 50 years start slower

21

However…

Anemia predisposes to intolerance

- watch for tachycardia, palpitations, nervousness
- correct low Hct (esp if below 28) before starting
- start low, 25 mcg or less

22

Levothyroxine

The levothyroxine sodium dose is generally adjusted in 12.5 to 25 mcg increments until the patient with primary hypothyroidism is clinically euthyroid and the serum TSH has normalized. Due to the long half-life of levothyroxine, the peak therapeutic effect at a given dose may not be attained for 4 to 6 weeks.

23

Levothyroxine Interactions

- Calcium
- Iron (including prenatal vitamins or other vitamin/mineral preps)
- Soy protein
  - all decrease absorption
  - separate by at least 2 hours (4 would be better)

24

Fentanyl Transdermal Patch

Only in opioid tolerance

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Opioid Tolerance

Patients with at least a week of

- morphine (oral) 60 mg daily
- oxycodone 30 mg daily
- hydromorphone (oral) 8 mg daily
- or an equianalgesic dose of another opioid

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Dose Titration

- Increase initial dose after 3 days
- Subsequent titrations should occur no more than every 6 days
- Until adequate analgesia is achieved
- Dose increases should be based on daily supplemental opioid dose using the ratio 45 mg/24 hr of oral morphine to a 12 mcg/hr increase in transdermal fentanyl

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A fentanyl transdermal patch (Duragesic®) releases a constant amount of fentanyl over:

A. 1 day
B. 2 days
C. 3 days
D. 7days

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Fentanyl Patch

- Replace patch every 48-72 hours
- Potential for abuse and associated risk of fatal overdose due to respiratory depression
- P450 3A4 inhibitors – can increase plasma concentrations of fentanyl

29

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30

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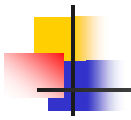
31



Dose Consistency

- Warfarin
- Insulin

32

FDA Alerts

33

September 28, 2009

FDA Drug Safety Communication: Sitagliptin linked to acute pancreatitis

34

- Between October 2006 and February 2009, a total of 88 cases of acute pancreatitis were reported in patients receiving sitagliptin, including two cases of hemorrhagic or necrotizing pancreatitis that required extensive hospitalization; four of these patients in the reports were admitted to the intensive care unit.

35

- In its review of the patients who developed pancreatitis, the FDA found that 19 (21%) of the 88 reported cases occurred within 30 days of starting sitagliptin or sitagliptin/metformin. When sitagliptin was discontinued, 47 (53%) of the 88 cases resolved.

36

The FDA noted other potential causes for pancreatitis in 45 cases (51%):

37

The FDA noted other potential causes for pancreatitis in 45 cases (51%):

- obesity

38

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- obesity
- high cholesterol

39

The FDA noted other potential causes for pancreatitis in 45 cases (51%):

- obesity
- high cholesterol
- high triglycerides

40

The FDA noted other potential causes for pancreatitis in 45 cases (51%):

- obesity
- high cholesterol
- high triglycerides
- diabetes

41

According to the safety recommendations for simvastatin released by the FDA in June 2011, the maximum dose of simvastatin should not exceed: (*Note: this does not include patients already established on a higher dose*)

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

42

Do not exceed _____ of simvastatin when given with amlodipine.

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

43

Do not exceed ___ of simvastatin when given with amiodarone. (*Note: This answer is based upon the December 2011 update*)

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

44

Do not exceed ___ of simvastatin when given with gemfibrozil.

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

45

The maximum dose of simvastatin when given with diltiazem is:

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

46

Simvastatin (Zocor®): Label Changes - New Restrictions, Contraindications, and Dose Limitations

Posted: 06/08/2011

47

FDA notified healthcare professionals that it is recommending limiting the use of the highest approved dose of the cholesterol-lowering medication simvastatin (80 mg) because of increased risk of muscle damage. Patients taking simvastatin 80 mg daily have an increased risk of myopathy compared to patients taking lower doses of this drug or other drugs in the same class. This risk appears to be higher during the first year of treatment, is often the result of interactions with certain medicines, and is frequently associated with a genetic predisposition toward simvastatin-related myopathy. The most serious form of myopathy, called rhabdomyolysis, can damage the kidneys and lead to kidney failure which can be fatal. FDA is requiring changes to the simvastatin label to add new contraindications (should not be used with certain medications) and dose limitations for using simvastatin with certain medicines.

48

Simvastatin

- Contraindicated
  - Itraconazole
  - Ketoconazole
  - Posaconazole
  - Erythromycin
  - Clarithromycin
  - Telithromycin
  - HIV protease inhibitors
  - Nefazodone
  - Gemfibrozil
  - Cyclosporine
  - Danazol

49

Simvastatin

- Contraindicated
  - Itraconazole
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  - Nefazodone
  - Gemfibrozil
  - Cyclosporine
  - Danazol

50

Simvastatin

- 10 mg/day
  - Diltiazem
  - Verapamil
- 20 mg/day
  - Amiodarone
  - Amlodipine
  - Ranolazine
- Grapefruit juice
  - Avoid > 1 quart/day

51

Simvastatin

- 10 mg/day
  - Diltiazem
  - Verapamil
- 20 mg/day
  - Amiodarone
  - Amlodipine
  - Ranolazine
- Grapefruit juice
  - Avoid > 1 quart/day

52

Lovastatin - Feb. 28, 2012

- Strong CYP3A4 inhibitors are contraindicated:
- Avoid
  - Cyclosporine
  - Gemfibrozil
- 20 mg/ day
  - Danazol
  - Diltiazem
  - Verapamil
- 40 mg
  - amiodarone
- Grapefruit juice
  - Avoid > 1 quart/day

53

Also from Feb. 28, 2012

- Added to Warnings:
  - memory problems
  - new onset diabetes
- Removed - recommendation for routine liver enzyme monitoring -

  Liver injury from statins is rare, and monitoring does not seem to be effective in predicting or preventing such damage.

54

According to the FDA, what dose of atorvastatin is approximately equivalent to rosuvastain 20 mg (for LDL lowering)?

A. 10 mg
B. 20 mg
C. 40 mg
D. 80 mg

55

Pedersen TR, Faergeman O, Kastelein JJ, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial [published correction appears in JAMA 2005 Dec 28;294(24):3092]. *JAMA* 2005;294(19):2437-2445. doi:10.1001/jama.294.19.2437

- Atorvastatin 80 mg compared to simvastatin 20 mg
- Could increase simvastatin to 40 mg if TC > 190
- Could decrease atorvastatin to 40 mg for ADRs
- 597 of 4449 decreased to 40 mg
- 49% LDL decrease in atorvastatin group at 12 weeks

56

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A. 10 mg
B. 20 mg
C. 40 mg
D. 80 mg

57

According to the FDA, what dose of atorvastatin is approximately equivalent to rosuvastain 20 mg (for LDL lowering)?

D. **80 mg**

58

3/28/2012

Abnormal heart rhythms associated with high doses of citalopram hydrobromide (Celexa®)

59

The U.S. Food and Drug Administration (FDA) is informing healthcare professionals and patients that the antidepressant Celexa® (citalopram hydrobromide; also marketed as generics) **should no longer be used at doses greater than 40 mg per day** because it can cause abnormal changes in the electrical activity of the heart. Studies did not show a benefit in the treatment of depression at doses higher than 40 mg per day.

60

Citalopram

- Maximum dose - 40 mg/day due to prolongation of QT interval
- Max of 20 mg/day:
  - over 60 years old
  - liver impairment
  - poor CYP2C19 metabolizers
  - taking cimetidine (Tagamet®)

61

Citalopram

- Not recommended for:
  - patients with CHF,
  - bradyarrhythmias,
  - concomitant use of medications that prolong the QT interval
- Monitor ECGs and electrolytes
- Discontinue if patient has persistent QTc measurements of >500 ms.

62

Linezolid

The U.S. Food and Drug Administration (FDA) has received reports of serious central nervous system (CNS) reactions when the antibacterial drug linezolid (marketed as Zyvox®) is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications).

63

Linezolid

- Inhibits monoamine oxidase A
- Results in decreased serotonin metabolism
- Serotonin toxicity = Serotonin syndrome
- Should avoid linezolid in patients taking serotonergic drugs unless treating:
  - VRE
  - Noscomial pneumonia
  - Complicated skin and skin structure infections (including MRSA)

64

Linezolid

- Emergent cases
  - Use alternate therapy for linezolid
  - Stop serotonergic drug and monitor patient for CNS toxicity for:
    - Two weeks (five with fluoxetine)
    - 24 hours after last dose of linezolid
    - whichever comes first

65

Linezolid

- Non-emergent cases
  - D/C serotonergic drug 2 weeks before starting linezolid (5 weeks for fluoxetine)
  - Resume serotonergic drug 24 hours after last dose of linezolid
  - Educate patient of signs and symptoms of Serotonin Syndrome
  - Report adverse events to FDA MedWatch

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Serotonergic Psychiatric Medications

- SSRIs
- SNRIs
- Tricyclics
- MAOIs
- Other:
  - Amoxapine
  - Maprotiline
  - Nefazodone
  - Trazodone
  - Buproprion
  - Buspirone
  - Vilazodone

67

Serotonin Syndrome Symptoms

- Tremor
- Altered mental status
- Clonus
- Muscular hypertonicity
- Hyperthermia

68

7/26/2011

Serious CNS reactions possible when methylene blue is given to patients taking certain psychiatric medications

69

The U.S. Food and Drug Administration (FDA) has received reports of serious central nervous system (CNS) reactions when the drug methylene blue is given to patients taking psychiatric medications that work through the serotonin system of the brain (serotonergic psychiatric medications). Methylene blue is commonly used in diagnostic procedures and is also used to treat a number of medical conditions.

70

Methylene Blue

- Monoamine oxidase inhibitor properties
- Urgent treatment of:
  - Methemoglobinemia
  - Ifosfamide-induced encephalopathy
  - Cyanide poisoning

71

Also

- Urinary medications
  - UTA
  - Urogesic blue
  - Uribel

72

1/10/2013

FDA Drug Safety Communication: Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem

73

FDA has informed the manufacturers that the recommended dose of zolpidem for **women** should be lowered from 10 mg to 5 mg for immediate-release products (Ambien®, Edluar®, and Zolpimist®) and from 12.5 mg to 6.25 mg for extended-release products (Ambien® CR). FDA also informed the manufacturers that, for **men**, the labeling should recommend that health care professionals consider prescribing the lower doses – 5 mg for immediate-release products and 6.25 mg for extended-release products.

74

5/14/2013

FDA Drug Safety Communication: FDA approves new label changes and dosing for zolpidem products and a recommendation to avoid driving the day after using Ambien® CR

75

The recommended initial dose of certain immediate-release zolpidem products (Ambien® and Edluar®) is 5 mg for women and either 5 mg or 10 mg for men. The recommended initial dose of zolpidem extended-release (Ambien® CR) is 6.25 mg for women and either 6.25 or 12.5 mg for men.

76

The recommended **initial** dose of certain immediate-release zolpidem products (Ambien® and Edluar®) is 5 mg for **women** and either 5 mg or 10 mg for **men**. The recommended initial dose of zolpidem extended-release (Ambien® CR) is 6.25 mg for women and either 6.25 or 12.5 mg for men.

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Zolpidem Recommendations

- use the lowest effective dose
- initial dose is 5 mg for women; either 5 or 10 mg for men
- recommended initial doses for women and men are different because zolpidem clearance is lower in women
- take once per night immediately before bedtime with at least 7-8 hours remaining before the planned time of awakening

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Zolpidem Recommendations

- if the 5 mg dose is not effective, increase to 10 mg
- higher morning blood levels following use of the 10 mg dose increase the risk of next day impairment of driving and other activities that require full alertness
- total dose of zolpidem should not exceed 10 mg once daily immediately before bedtime

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Zolpidem **Extended Release** Recommendations

- caution patients against driving and other activities requiring complete mental alertness the **day after** use
- impairment can be present despite feeling fully awake

80

Patient Counseling

- tell patients that zolpidem has the potential to cause next-day impairment
- risk is increased if dosing instructions are not carefully followed
- wait at least 8 hours after dosing before driving or engaging in other activities requiring full mental alertness
- impairment can be present despite feeling fully awake

81

April 30, 2019

FDA requires stronger warnings about rare but serious incidents related to certain prescription insomnia medicines

- **Eszopiclone**
- **Zaleplon**
- **Zolpidem**

82

Complex Sleep Behaviors

Several reports of rare, but serious injuries and deaths

- Sleepwalking
- Sleep driving
- Unsafely using a stove

Contraindication - Do not use these medicines in patients who have experienced an episode of complex sleep behaviors after taking them.

83

7/26/2013

FDA Drug Safety Communication: FDA limits usage of ketoconazole (Nizoral®) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems

84

(FDA) is taking several actions related to Nizoral (ketoconazole) oral tablets

- limiting the drug's use
- warning that it can cause severe liver injuries
- adrenal gland problems
- can lead to harmful drug interactions
- should only for endemic mycoses
- only when alternative antifungal therapies are not available or tolerated.

85

Keep in mind -

It is sometimes used because of its anti-andrenal activity such as in adrenal hyperplasia or Cushing's disease

86

March 4, 2020

FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair®); advises restricting use for allergic rhinitis

Risks may include suicidal thoughts or actions

87

The U.S. Food and Drug Administration (FDA) is strengthening existing warnings about serious behavior and mood-related changes with montelukast (Singulair® and generics), which is a prescription medicine for asthma and allergy.

88

FDA Recommendations

- For allergic rhinitis, also known as hay fever, we have determined that montelukast should be reserved for those who are not treated effectively with or cannot tolerate other allergy medicines.
- For patients with asthma, we recommend that health care professionals consider the benefits and risks of mental health side effects before prescribing montelukast.

89

FDA Recommendations for Consumers

Patients and parents/caregivers should stop montelukast and discuss with a health care professional right away if you or your child experiences behavior or mood-related changes while taking the medicine.

90

These may include:

- agitation, including aggressive behavior or hostility
- attention problems
- bad or vivid dreams
- depression
- disorientation or confusion
- feeling anxious
- hallucinations
- irritability
- memory problems
- obsessive-compulsive symptoms
- restlessness
- sleepwalking
- stuttering
- suicidal thoughts and actions
- tremor or shakiness
- trouble sleeping
- uncontrolled muscle movements

91

FDA Recommendations for Consumers

- You should take montelukast for allergic rhinitis or hay fever only if you cannot tolerate other medicines or they do not work for you. Many other safe and effective allergy medicines are widely available, including over-the-counter medicines without a prescription.
- Talk to your pharmacist or healthcare professional for help deciding which might be best.

92

FDA Recommendations for Consumers

- You should take montelukast for allergic rhinitis or hay fever only if you cannot tolerate other medicines or they do not work for you. Many other safe and effective allergy medicines are widely available, including over-the-counter medicines without a prescription.
- Talk to your **pharmacist** or healthcare professional for help deciding which might be best.

93

FDA Recommendations for Healthcare Professionals

Health care professionals should consider the risks and benefits of montelukast when deciding to prescribe or continue patients on the medicine.

94

Monthly Consults

Should we recommend stopping montelukast for allergic rhinitis?

95

- Some are theorizing targeting leukotrienes to attenuate cytokine storm seen in COVID-19

96

- Some are **theorizing** targeting leukotrienes to attenuate cytokine storm seen in COVID-19
- Published clinical trial evidence in COVID-19 is sparse
  - Mixed results

97

Patil T, Raguindin JJ, Radtke M, Smigiel J, Savona N, Kavuru B, Sekhri A. Evaluating the Association of Montelukast Use on Neuropsychiatry-Related Healthcare Utilization and Depression in COVID-19-Hospitalized Veterans: A Nationwide VA Observational Cohort Study. Clin Drug Investig. 2023 Aug;43(8):605-619. doi: 10.1007/s40261-023-01292-5. Epub 2023 Jul 27. PMID: 37498493.

98

Patil, et al, Clin Drug Investig. 2023 Aug;43(8):605-619.

415 Monteleukast

409 No monteleukast

"Patients with prior montelukast use who were hospitalized with COVID-19 appeared to have increased rate of neuropsychiatry-related healthcare utilization."

Monteleukast vs no monteluekast	no difference
New depression or new antidepressant	no difference

99

Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. *J Allergy Clin Immunol*. 2020;146(4):721-767. doi:10.1016/j.jaci.2020.07.007 (AAAAI)

- Monotherapy, Allergic (AR) – nasal steroid (INCS)
- Monotherapy, Nonallergic (NAR) – either INCS or nasal antihistamine
- Can consider INCS, nasal antihistamine combo for allergic or non-allergic
- Montelukast should only be used for AR if there has been an inadequate response or intolerance to alternative therapies
- For persitant rhinorrhea – can offer ipratropium for perennial AR or NAR
- If using oral antihistamine – 2nd generation over 1st

100

Keep in mind -

- Inhaled and intranasal corticosteroids can increase intraocular pressure (IOP)
- Patients with glaucoma may need to avoid or access affect on IOP for possible glaucoma medication dose adjustment

101

Bundhun PK, et al. BMC Cardiovasc Disord. 2017 Jan 5;17(1):3. doi: 10.1186/s12872-016-0453-6.

Is the concomitant use of clopidogrel and Proton Pump Inhibitors still associated with increased adverse cardiovascular outcomes following coronary angioplasty?: a systematic review and meta-analysis of recently published studies (2012 - 2016)

https://pubmed.ncbi.nlm.nih.gov/28056809/

102

Bundhun PK, et al. BMC Cardiovasc Disord. 2017 Jan 5;17(1):3. doi: 10.1186/s12872-016-0453-6.

The combined use of clopidogrel with PPIs is still associated with significantly higher adverse cardiovascular events such as MACEs, ST and MI following PCI supporting results of the previously published meta-analysis. However, long-term mortality is not statistically significant warranting further analysis with randomized patients.

103

Bundhun PK, et al. BMC Cardiovasc Disord. 2017 Jan 5;17(1):3. doi: 10.1186/s12872-016-0453-6.

Is the concomitant use of clopidogrel and Proton Pump Inhibitors still associated with increased adverse cardiovascular outcomes following coronary angioplasty?: a systematic review and meta-analysis of recently published studies (2012 - 2016)

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104

Bowry AD, et al. *Am J Cardiol*. 2008;101(7):960-966. doi:10.1016/j.amjcard.2007.11.057

MA of 8 studies N=91,744)

Compared with aspirin alone, dual therapy with aspirin and clopidogrel reduced the odds ratio of the composite outcome of death, reinfarction, and stroke by 15% (95% CI 23% to 6%) in patients with acute coronary syndromes and by 34% (95% CI 44% to 22%) in patients who underwent percutaneous coronary intervention. Dual therapy also significantly reduced the odds of fatal and nonfatal reinfarction in these patient groups but did not significantly reduce the odds of all-cause mortality.

105

Clopidogrel

- Ranitidine
- Famotidine
- Pantoprazole
- Rabeprazole

106

July 26, 2016

FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together

107

Black Box Warning

Potentially permanent side effects:

- Tendons
- Muscles
- Joints
- Nerves
- central nervous system

that can occur together in the same patient.

108

Risks generally outweigh benefits

- acute bacterial sinusitis (ABS)
- acute bacterial exacerbation of chronic bronchitis (ABECB)
- uncomplicated urinary tract infections (UTI)

In these situations, reserve for use when there are no other options

109

July 10, 2018

FDA reinforces safety information about serious low blood sugar levels and mental health side effects with fluoroquinolone antibiotics; requires label changes

110

Mental Health Side Effects

- Disturbances in attention
- Disorientation
- Agitation
- Nervousness
- Memory impairment
- Delirium

111

December 20, 2018

FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients

112

Fluoroquinolones should not be used in patients at increased risk unless there are no other treatment options available.

- history of blockages or aneurysms (abnormal bulges) of the aorta or other blood vessels
- high blood pressure
- certain genetic disorders that involve blood vessel changes
- the elderly

113

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- the elderly

114

Levofloxacin labeling changes 5/3/2019

5.9 Risk of Aortic Aneurysm and Dissection

Epidemiologic studies report an increased rate of aortic aneurysm and dissection within two months following use of fluoroquinolones, particularly in elderly patients. The cause for the increased risk has not been identified. In patients with a known aortic aneurysm or patients who are at greater risk for aortic aneurysms, reserve LEVAQUIN® for use only when there are no alternative antibacterial treatments available.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020634s072lbl.pdf

115

Levofloxacin

- Common side effects:
  - confusion
  - insomnia
  - dysglycemia – in diabetics
    - hypoglycemia first 2 to 3 days
    - hyperglycemia after that
  - phototoxicity

116

Levofloxacin

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  - **phototoxicity**

117

Other Photosensitizing Drugs

- HCTZ
- Sulfamethoxazole/trimethoprim
- Sulfonylureas
- Tetracyclines
- St. John's Wort

118

Other Photosensitizing Drugs

- HCTZ
- Sulfamethoxazole/trimethoprim
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- Tetracyclines
- St. John's Wort

119

Photosensitizing Drugs

Pedersen SA, et al. Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. *J Am Acad Dermatol*. 2018;78(4):673-681.e9. doi:10.1016/j.jaad.2017.11.042

Conclusion: Hydrochlorothiazide use is associated with a substantially increased risk of NMSC, especially SCC.

120

Photosensitizing Drugs

Friedman GD, et al. Antihypertensive drugs and lip cancer in non-Hispanic whites. *Arch Intern Med*. 2012;172(16):1246-1251. doi:10.1001/archinternmed.2012.2754

Conclusion: These data support an increased risk of lip cancer in non-Hispanic whites receiving treatment for hypertension with long-term use of photosensitizing drugs.

121

Photosensitizing Drugs

- Use
  - sunscreen
  - sunglasses
  - lip balm

122

Other Photosensitizing Drugs

- HCTZ
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123

Other Photosensitizing Drugs

- HCTZ
- Sulfamethoxazole/trimethoprin
- Sulfonylureas
- Tetracyclines
- St. John's Wort

124

Doxycycline

- Photosensitivity precautions
- More forgiving of calcium than most in class
- Empty stomach instructions could be mean

125

Doxycycline – package insert

If gastric irritation occurs, it is recommended that doxycycline be given with food or milk. The absorption of doxycycline is not markedly influenced by simultaneous ingestion of food or milk.

126

Doxycycline – package insert

Esophagitis and esophageal ulcerations have been reported in patients receiving capsule and tablet forms of the drugs in the tetracycline class. Most of these patients took medications immediately before going to bed.

127

Doxycycline – package insert

Administration of adequate amounts of fluid along with capsule and tablet forms of drugs in the tetracycline class is recommended to wash down the drugs and reduce the risk of esophageal irritation and ulceration.

128

Anticholinergic Drugs

A drug interaction of note

129

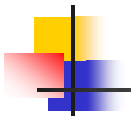
All solid oral dosage forms of potassium chloride are contraindicated in any patient in whom there is structural, pathological (e.g., diabetic gastroparesis), or pharmacologic (use of anticholinergic agents or other agents with anticholinergic properties at sufficient doses to exert anticholinergic effects) cause for arrest or delay in tablet passage through the gastrointestinal tract.

130

Prepare an aqueous (water) suspension as follows:

- Place the whole tablet(s) in approximately one-half glass of water (4 fluid ounces).
- Allow approximately 2 minutes for the tablet(s) to disintegrate.
- Stir for about half a minute after the tablet(s) has disintegrated.
- Swirl the suspension and consume the entire contents of the glass immediately by drinking or by the use of a straw.
- Add another one fluid ounce of water, swirl, and consume immediately.
- Then, add an additional one fluid ounce of water, swirl, and consume immediately.

131



Anticholinergic Drugs

Toxidrome mneumonic

- Blind as a bat
- Dry as a bone
- Mad as a hatter
- Hot as a hare
- Red as a beet

132

Counseling Points

- Blind as a bat –
  - blurry vision
  - dilated pupils
  - caution with driving
  - recommend sunglasses
- Dry as a bone
  - decreased saliva
  - increased risk of cavities
  - recommend dental exams
- Mad as a hatter
  - confusion
  - memory loss

133

Counseling Points

- Hot as a hare
- Red as a beet

- Both are associated with heat intolerance
- Counsel about heat precautions

134

Anticholinergics - Uses

- GI
  - dicyclomine
  - hyoscyamine
- Overactive bladder
  - oxybutynin
  - tolterodine
  - darefenacin
  - solefenacin

135

Anticholinergics - Uses

- Excessive salivation
  - glycopyrrolate
  - atropine
  - scopolamine
- Antipsychotic induced EPS
  - benztropine
  - trihexyphenidyl

136

Antidepressants

- Amitriptyline
- Desipramine
- Doxepin
- Imipramine
- Nortriptyline
- Paroxetine

137

Antipsychotics

- Chlorpromazine
- Clozapine
- Olanzapine
- Quetiapine

138

Antihistamines

- Diphenhydramine
- Brompheniramine
- Chlorpheniramine
- Hydroxyzine
- Meclizine
- Promethazine

139

Others

- Methocarbamol
- Orphenadrine
- Cyclobenzaprine

- Carbamazepine
- Oxcarbazepine

140

Other agents with potential for heat intolerance

- Amphetamines
- Pseudoephedrine
- Phenylepherine
- ACEi's/ARB's
- Diuretics
- Zonisamide
- Topiramate

141

Topiramate

- Seems to decrease aquaporin 5 expression
- Aquaporins 1-4: primarily renal activity
- Aquaporin 5
  - sweat
  - saliva
  - tears
  - pulmonary secretions

142

Other Side Effects with Topiramate

- Taste disturbances
- Confusion
- Word-finding difficulties
- Loss of appetite
- Visual disturbances

143

Kalisch Ellett, L.M., Pratt, N.L., Le Blanc, V.T., Westaway, K. and Roughead, E.E. (2016), Increased risk of hospital admission for dehydration or heat-related illness after initiation of medicines: a sequence symmetry analysis. J Clin Pharm Ther, 41: 503-507. doi:10.1111/jcpt.12418

144

Kalisch Ellett, et al Sequence Ratios

- **ACEi + diuretic** **2·79** (1·53–4·43)
- **ACEi / ARB** **1·88** (1·55–2·26)
- **Diuretics** **1·83** (1·58–2·11)
- **ARB + diuretic** **1·78** (1·22–2·46)
- **ACEi plain** **1·59** (1·31–1·90)

145

Other medications with potential for heat related illness

- ACEi's/ARB's - Impaired thirst sensation
- Diuretics - decreased sodium, dehydration
- ß-blockers - reduced blood flow to the skin
- SSRI's - hyponatremia, impaired temperature regulation
- CNS depressants – impaired environmental awareness

146

Other medications with potential for heat related illness

- ACEi's/ARB's - Impaired thirst sensation
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ARB Distinguishing Traits

- Losartan - lowers uric acid
- In general, other ACEi's and ARB's seem to raise it
- Losartan might be preferred in a patient with gout
- Irbesartan might be a second choice

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ARB Distinguishing Traits

- Olmesartan (Benicar®)
- FDA alert: symptoms of sprue-like enteropathy, which include severe, chronic diarrhea with substantial weight loss
- The enteropathy may develop months to years after starting olmesartan, and sometimes requires hospitalization

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ARB Distinguishing Traits

- Candesartan (Atacand®)
- Has shown benefit in migraine prevention
- Has shown some benefit in preventing occurrence of DM2

150

Trigger Drugs/Diagnoses

- My term
- Seeing a particular drug or diagnosis makes you look for or at something else

151

Thiamine

- B vitamin (B_1)
- water soluble
- B vitamins – important for energy production at the cellular level
- Vitamin B_1 deficiency –> beri beri

152

Beri Beri

- Dry – neuropathy
  - peripheral
  - cerebral – Wernicke-Korsakoff
- Wet
  - cardiac

153

Thiamine – potential uses

- High dose diuretic – particularly loop diuretics
- Hepatitis B

154

Vitamin C

- Ascorbic acid
- Water soluble
- Fruits and vegetables
- Antioxidant
- Collagen and tissue repair
- RDA - 60 mg

155

Vitamin C
RSD Prevention

- Randomized, double-blind, placebo-controlled,
- 117 adult patients (79%) female
  - Vit C 500 mg/day X 50 days (52 pts. w/54 fx)
  - Placebo daily X 50 days (63 pts. w/65 fx)

Zollinger, et al. *Lancet 1999;354:2025-2028*

156

AAOS Guidelines for Wrist Fracture (2010)

We suggest adjuvant treatment of distal radius fractures with Vitamin C for the prevention of disproportionate pain.

Strength of Recommendation: Moderate

157

AAOS Guidelines for Wrist Fracture (2010)

We suggest adjuvant treatment of distal radius fractures with Vitamin C for the prevention of disproportionate pain.

Strength of Recommendation: Moderate

Update
2021 Guideline does not include this recommendation

It is not part of the PICO (Population, Intervention, Comparison, Outcome) question list, so not addressed at all

158

Other Triggers

159

Other Triggers

Patient on:

methotrexate

Make sure also on:

folic acid

160

Other Triggers

Patient on:

long term, systemic glucocorticoids

Make sure also has:

bone protection strategies

161

Other Triggers

Patient gets Rx for:

dextromethorphan

Make sure not on:

SSRI's; SNRI's

162

Other Triggers

Patient on:

clopidogrel

Make sure not on:

omeprazole, esomeprazole

163

Other Triggers

Patient on:

oral, solid potassium

Make sure not on:

anticholinergic agent

164

Other Triggers

Look for patterns in your practice site

165

According to the safety recommendations for simvastatin released by the FDA in June, 2011, the maximum dose of simvastatin should not exceed: (Note: this does not include patients already established on a higher dose.)

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

166

Do not exceed _____ of simvastatin when given with amlodipine.

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

167

Do not exceed ___ of simvastatin when given with amiodarone. (Note: This answer is based upon the December 201 update.)

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

168

Do not exceed ___ of simvastatin when given with gemfibrozil.

A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

169

The maximum dose of simvastatin when given with diltiazem is:

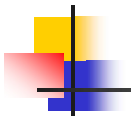
A. 0 mg (Do not use)
B. 10 mg
C. 20 mg
D. 40 mg
E. 80 mg

170

Community and/or distributive pharmacists commonly have the opportunity to practice clinical pharmacy.

A. True
B. False

171



Remember!

- There will be many opportunities to help patients
- Remember why we are here
- We have an important role in the safe, appropriate, and cost-effective use of medications

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