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FACULTY: Bryan D. Hayes, PharmD, FAACT, FASHP

Assistant Professor of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School

PRESENTATION

Black Box Drugs We Use: What's the Risk?

DESCRIPTION

The black box drug list seems to be growing yet we are constantly faced with drug shortages limiting choices when caring for patients in the emergency department. Many have used these drugs extensively in the past and feel quite comfortable with continuing this use on patients. What is our risk when we do this? Is it a reasonable risk?

The speaker will summarize black box warnings on drugs frequently used in the emergency department, assess the risk of this continued use, justify appropriate use in specific patients, and identify critical documentation needed when choosing to use these drugs.

OBJECTIVES

- Summarize black box warnings on drugs frequently used when caring for patients in the emergency department.
- Assess the risk of continued use of these drugs despite these warnings.
- Justify appropriate continued use of black box drugs in the context of specific patients presented through a case-based approach.
- For each drug/drug class, 1) the problem, 2) the data, 3) where is used within the emergency department, and 4) the verdict of it is safe to use.
- Topics discussed will be fluoroquinolones, tramadol, droperidol, midazolam + olanzapine, NSAIDs, and ondansetron.

DISCLOSURE

No significant financial relationships to disclose.

Black Box Drugs We Use: What's the Risk?

Bryan D. Hayes @PharmERToxGuy





"Serious or life-threatening risk"

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use AVELOX[®] safely and effectively. See full prescribing information for AVELOX.

AVELOX[®] (moxifloxacin hydrochloride) Tablet, film-coated AVELOX[®] (moxifloxacin hydrochloride) Injection, solution for IV use Initial U.S. Approval: 1999

To reduce the development of drug-resistant bacteria and maintain the effectiveness of AVELOX and other antibacterial drugs, AVELOX should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

WARNING:

Fluoroquinolones, including AVELOX[®], are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants *[see Warnings and Precautions (5.1)]*.

Address:	Date:
R R 37% boxec	consider I warnings
MD:	
Signature:	

Smollin CG, et al. J Med Toxicol 2016;12:180-4.



FLUOROQUINOLONES





Seizures

Neuropsychiatric Effects

Myas he ia iravis

Peripheral Neuropathy



RR 2.07

Etminan M, et al. *Neurology* 2014;83:1261-3. Francis JK, et al. *J Investig Med High Impact Case Rep* 2014;2(3).



QT Prolongation

Moxifloxacin > Azithromycin



aHR 3.44

Pépin J, et al. *Clin Infect Dis* 2005;41(9):1254-60. Sarma JB, et al. *J Hosp Infect* 2015;91(1):74-80.

Aortic Dissection/Aneurysm



RR 2.43

Lee CC, et al. JAMA Intern Med 2015;175(11):1839-47.

Hyperglycemia (up to 7/1,000)

Hypoglycemia (up to 10/1,000)



Retinal Detachment (RR 4.5)

Etminan M, et al. JAMA 2012;307:1414-9. Raguideau F. JAMA Ophthalmol 2016;134:415-21.

ED, ED Obs, Inpatient Boarders, Discharge Rx



NO ALTERNATIVES

Uncomplicated UTI

Acute bacterial exacerbation of chronic bronchitis

Acute bacterial sinusitis













TRAMADOL

8 boxed warnings!





Just told 200 medical students tramadol is the Donald Trump of pain medicines: dangerous, irrational, and you're going to regret it

11:17 AM - 21 Nov 2016





Respiratory Depression Accidental Ingestion NAS Concomitant benzos

Abuse Dependence Withdrawal



Senay EC, et al. Drug Alcohol Depend 2003;69(3):233-41.

'Messy' pharmacology

Erratic metabolism

Young JW, et al. *CMAJ* 2013;185(8):E352. Leppert W. *Pharmacology* 2011;87(5-6):274-85.

Prevalence of Tramadol Consumption in First Seizure Patients: a One-Year Cross-Sectional Study

Asadi P, et al. Emerg (Tehran) 2015;3:159-61.

22% of first-seizure pts had recent tramadol use

- 1. Mean total tramadol dose in last 24 hours: 140 mg
- 2. Duration of tramadol use less than 10 days: 84.5%
- 3. Seizure within 6 hours of tramadol consumption: 74%

Hypoglycemia

OR 2.61

Fournier JP, et al. JAMA Intern Med 2015;175(2):186-93.

DOES IT WORK?

Osteoarthritis: modest

Neuropathic: comparable to alternatives

Cepeda MS, et al. *Cochrane Database Syst Rev* 2006;(8):CD005522. Hollingshead J, et al. *Cochrane Database Syst Rev* 2006;(3):CD003726.

IN THE ED

MS: < hydroc/APAP

Ankle: = hydroc/APAP

Turturro MA, et al. *Ann Emerg Med* 1998;32(2):139-43. Hewitt DJ, et al. *Ann Emerg Med* 2007;49(4):468-80.

ED Obs, Inpatient Boarders, Discharge Rx





MBAR





N/V CHS

Migraine Agitation



277 reports > 65 cases > 2 possible

Jackson CW, et al. Am J Health Syst Pharm 2007;64:1174-86.

273 OR cases reported (1997-2002)

Droperidol ≤ 1.25 mg

10 serious cardiovascular events (2 deaths)

No cause and effect

Habib AS, et al. Anesth Analg 2003;96:1377-9.

N/V 1.25 mg Migraine 2.5 CHS 1.25-2.5 mg Agitation 5-10

Electrolyte

Other QT meds

Cardiac

个 age







"Droperidol is an *effective and safe medication* in the treatment of nausea, headache, and agitation. The literature search did not support mandating an electrocardiogram or telemetry monitoring for doses < 2.5 mg given either IM or IV. IM doses of up to 10 mg of droperidol seem to be as safe and as effective as other medications used for sedation of agitated patient."



Calver L, et al. Ann Emerg Med 2015;66:230-8.



$0.625 \text{ mg} \rightarrow 1.25 \text{ mg} \rightarrow 2.5 \text{ mg}^*$ *Except agitation





MidazolamLorazepamDiazepam

H21

GABA

GABA Opioids - Midazolam Lorazepam Diazepam H2

OH

Opioids - Midazolam - V resp Lorazepam Diazepam

GABA

Monitored Setting

httphtphtphtpht "].

10

PRESS

TEMP

PRESS

SpO,/PLETH

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№ 139 0 st-111 № 09

26

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POWE





IV/IM Olanzapine

IV/IM Benzodiazepine

Marder SR, et al. J Clin Psychiatry 2010;71:433-41.

Case reports of postmarketing adverse event experiences with olanzapine intramuscular treatment in patients with agitation

Marder SR, et al. J Clin Psychiatry 2010;71(4):433-41.

Jan 2004 – Sep 2005 160 cases

29 fatalities 66% concomitant benzos



ED, ED Obs, Inpatient Boarders





NSAIDS (ketorolac, ibuprofen, naproxen)



Cardiovascular thrombotic events

Naproxen safest

Coxib and traditional NSAID Trialists' (CNT) Collaboration, et al. Lancet 2013;382:769-79.

CV disease



Male gender

Duration/dose





Gl Bleeding Ulceration Perforation

OR: 5.1

Savage RL, et al. Arthritis Rheum 1993;36:84-90.

Anticoagulant/ antiplatelet

Duration > 7d

Steroids

↑ age





ED, ED Obs, Inpatient Boarders, Discharge Rx





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Bryan D. Hayes, PharmD, FAACT, FASHP Assistant Professor of EM Harvard Medical School/MGH bryanhayes13@gmail.com @PharmERToxGuy PharmERToxGuy.com