Paying the Piper: Strategies for managing high cost antidotes

Background

Reasons

Pharmacoeconomics

Risks vs Benefits

Jeanna M. Marraffa, Pharm.D., DABAT, FAACT
Upstate New York Poison Center, Upstate Medical University
Syracuse NY

I have no financial disclosures to report

Background

- Large increase in price of medications
- Antidote price increases not immune to this
- Ongoing drug shortages

Objectives

- Identify some factors that drive the cost of antidotes
- Recognize the costs associated with the use of specific antidotes
- Identify resources available to determine what patients require antidotal therapy
- Recognize the role of the poison center in assisting in the stocking of antidotes as well as patient specific management

The Impact to poisoned patients

- Reduction in hospital stocking antidotes
- AWP increase of > 50% for 15 out of 33 antidotes
- Stocking price increased by > $1000 for 8 out of 33 antidotes

Where We've Felt it Most

Antidote	2010 AWP $	2015 AWP $	% Change
Edetate Calcium Disodium 6 grams	746	40,391	5308
Methylene blue 900 mg	59	1,118	1786
Protamine 200 mg	8	35	341
Digoxin immune FAB 100 mg	18,213	76,3210	319
Naloxone IV 15 mg	153	317	107
Succimer 86 grams	7,692	13,291	73

Adapted from: Heindel GA et al Clin Tox 2017

TOXICOLOGY/CONCEPTS

Expert Consensus Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care

Richard C. Dart, MD, PhD; Lewis R. Goldfrank, MD; Brian L. Erstad, PharmD; David T. Huang, MD, MPH; Knox H. Todd, MD, MPH; Jeffrey Weitz, MD; Vikhyat S. Bebarta, MD; E. Martin Caravati, MD, MPH; Fred M. Henretig, MD; Theodore R. Delbridge, MD, MPH; William Banner, MD, PhD; Sandra M. Schneider, MD; Victoria E. Anderson, MPH*

*Corresponding Author. E-mail: victoria.anderson@rmpdc.org.

- Is the antidote effective?
- Do the benefits outweigh its risks?
- Is time an important factor?
- Does the antidote need to be immediately available?
- Does the antidote need to be available within 60 minutes?
- What amount of the antidote is needed to treat one 100 kg patient?

Dart et al. Ann Emerg Med 2017

TOXICOLOGY/CONCEPTS

Expert Consensus Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care

Richard C. Dart, MD, PhD; Lewis R. Goldfrank, MD; Brian L. Erstad, PharmD; David T. Huang, MD, MPH; Knox H. Todd, MD, MPH; Jeffrey Weitz, MD; Vikhyat S. Bebarta, MD; E. Martin Caravati, MD, MPH; Fred M. Henretig, MD; Theodore R. Delbridge, MD, MPH; William Banner, MD, PhD; Sandra M. Schneider, MD; Victoria E. Anderson, MPH*

*Corresponding Author. E-mail: victoria.anderson@rmpdc.org.

- 45 antidotes were considered for stocking
- 2447 articles were utilized to develop the recommendations

- 44 antidotes were recommended to be stocked
  - 17 antidotes added from previous recommendations
- 23 antidotes recommended for immediate availability
  - Opioid poisoning
  - Cardiac glycoside toxicity
  - Cyanide poisoning
  - Methemoglobinemia
- 14 antidotes recommended within 60 minutes

Dart et al. Ann Emerg Med 2017

Paying the Piper: Strategies for managing high cost antidotes

Background

Reasons

Pharmacoeconomics

Risks vs Benefits

Jeanna M. Marraffa, Pharm.D., DABAT, FAACT
Upstate New York Poison Center, Upstate Medical University
Syracuse NY

I have no financial disclosures to report

What Factors Are Involved?

What Factors Are Involved?

Why do drugs cost what they cost?

- Research and Development
- Marketing
- Licensing Fees to FDA
- Liability Fees to FDA

- Low Utilization Drugs
- Orphan Drugs

"Hidden" Fees

- Prescription Drug User Fee Act (PDUFA) in 1992
  - Authorized the FDA to collect fees for its review for new drugs
- Numerous other fees including inspection and registration activities

- New Drug Application PDUFA: $2,374,200
  - New Drug Application Establishment: $585,200
  - Annual Product Registration: $114,450
- Generic Drug User Fee Act (GDUFA): $76,030
- Liability Fees: upwards of $500,000

Paying the Piper: Strategies for managing high cost antidotes

Background

Reasons

Pharmacoeconomics

Risks vs Benefits

Jeanna M. Marraffa, Pharm.D., DABAT, FAACT
Upstate New York Poison Center, Upstate Medical University
Syracuse NY

I have no financial disclosures to report

Is it only the Price Tag?

- Direct costs
- Indirect costs
- Reimbursement fees

Pharmacoeconomics

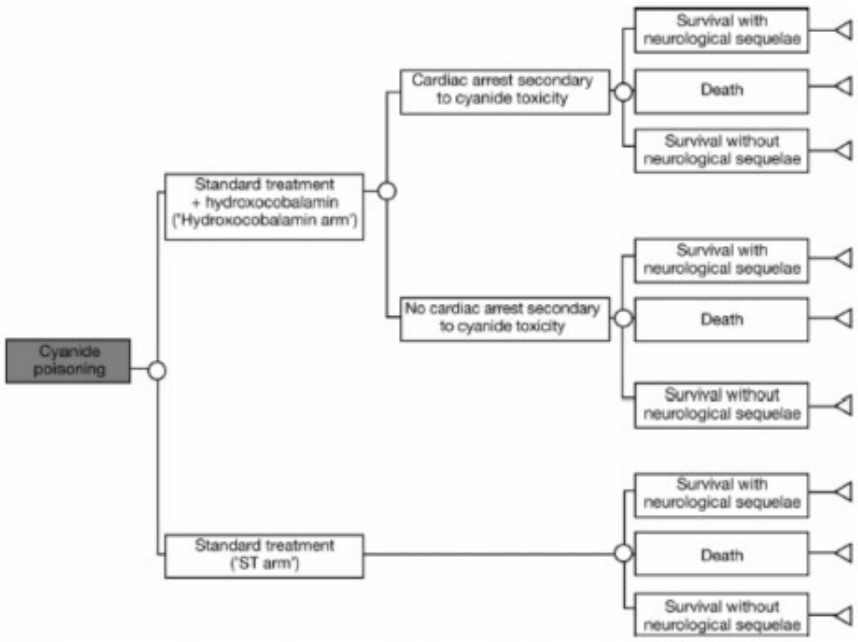
Concepts:

- Cost-benefit
- Cost-effectiveness
- Cost-minimization
- Cost of illness
  - Cost of adverse drug events
- Cost-utility

Arenas-Guzman R et al. J Eur Acad Dermatol Venereol 2005; 19 Suppl 1:34-39
DiMasi JA et al. Pharmacoeconomics 2001; 19(7): 753-766

Antidotes & Pharmacoeconomic Comparison

Decision Tree Analysis



Drieskens S, *et al*. *Eur J Hosp Pharm* 2013;**0**:1–7. doi:10.1136/ejhpharm-2012-000213

Antidotes & Pharmacoeconomic Comparison

Antidote	Cost Analysis	Conclusions
NAC	• IV versus PO comparison • Total cost associated with hospital stay	• PO > IV for hospital stay • 7 days vs. 4 days • $18,287.63 vs $7,607.82
Hydroxocobalamin	• Treatment vs standard treatment	• Hydroxcobalamin could save 17 lives per year • Better neurologic outcomes and less death • "Acceptable" levels of cost effectiveness
Fomepizole	• Compared the cost per adverse drug event avoided • Fomepizole versus ethanol	• Cost Effectiveness ratio • $10,521 for ethanol • $5,169 for fomepizole

1. Martello JL et al. Cost minimization analysis comparing enteral NAC to IV NAC in the management of acute acetaminophen toxicity. Clin Tox 2010; 48: 79-81
2. Drieskens S et al. Belgian cost effectiveness analysis of hydroxocobalamin in known or suspected cyanide poisoning. Eur J Hosp Pharm 2013; 0:1-7
3. Marraffa JM et al. Cost-effectiveness of fomepizole versus ethanol in the management of acute ethylene glycol exposure. Clinical Toxicology 2005; 43(6): 691.

Paying the Piper: Strategies for managing high cost antidotes

Background

Reasons

Pharmacoeconomics

Risks vs Benefits

Jeanna M. Marraffa, Pharm.D., DABAT, FAACT
Upstate New York Poison Center, Upstate Medical University
Syracuse NY

I have no financial disclosures to report

What if cost didn't matter?

- Efficacy
- Risk of ADRs
- Utility of certain antidotes

Some Cases for Consideration

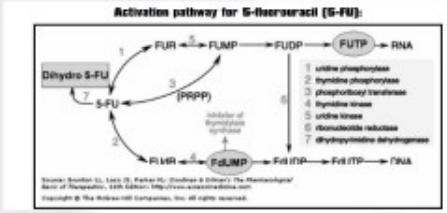
2 year old male is found with an empty tube of Efudex(R) 5%. The tube was originally 40 grams and was full.

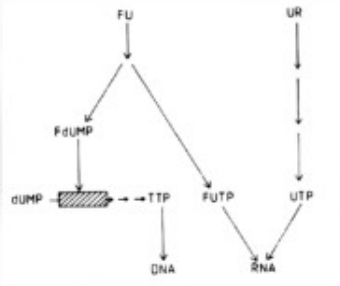
The ingestion occurred approximately 30 minutes earlier.

What would you do?

5-Fluorouracil

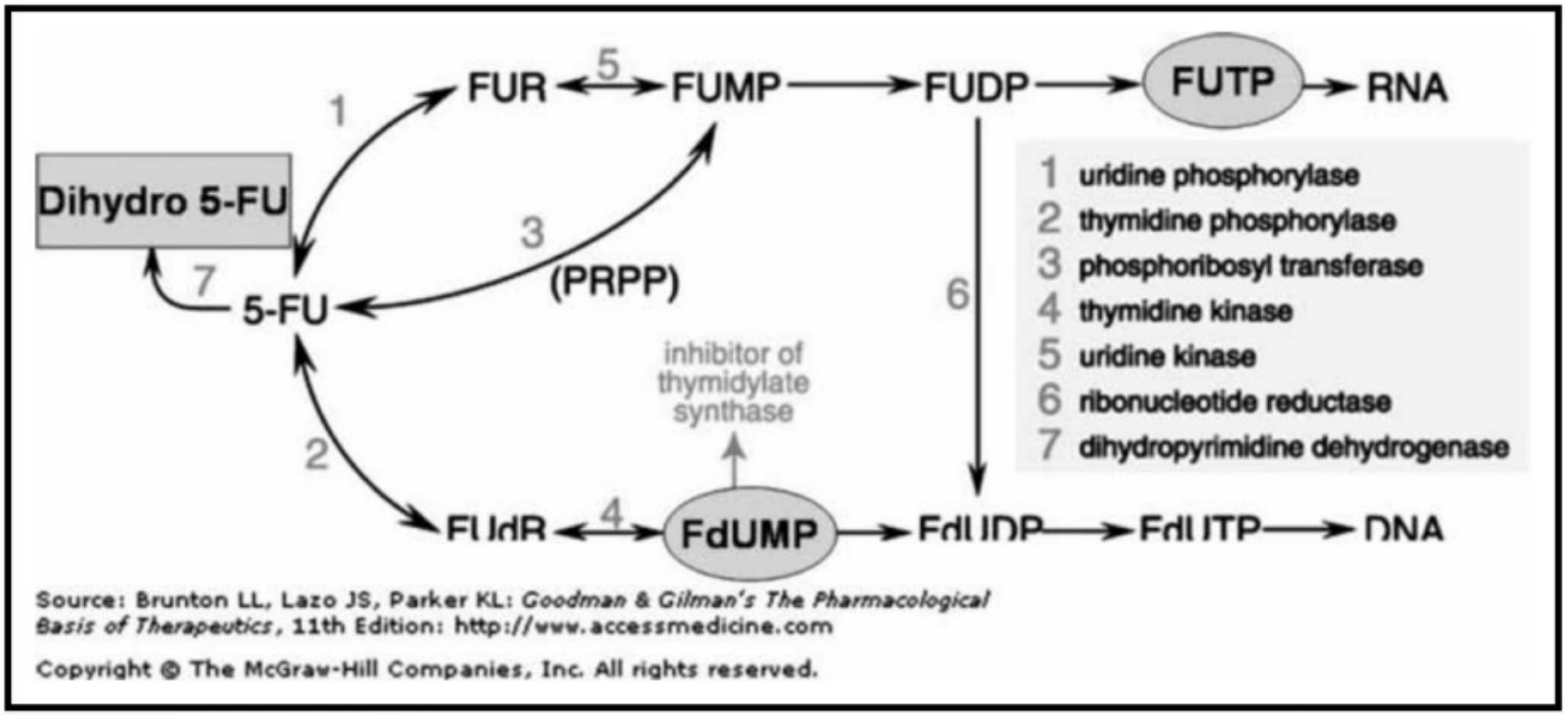
Doses > 5 mg/kg result in severe toxicity



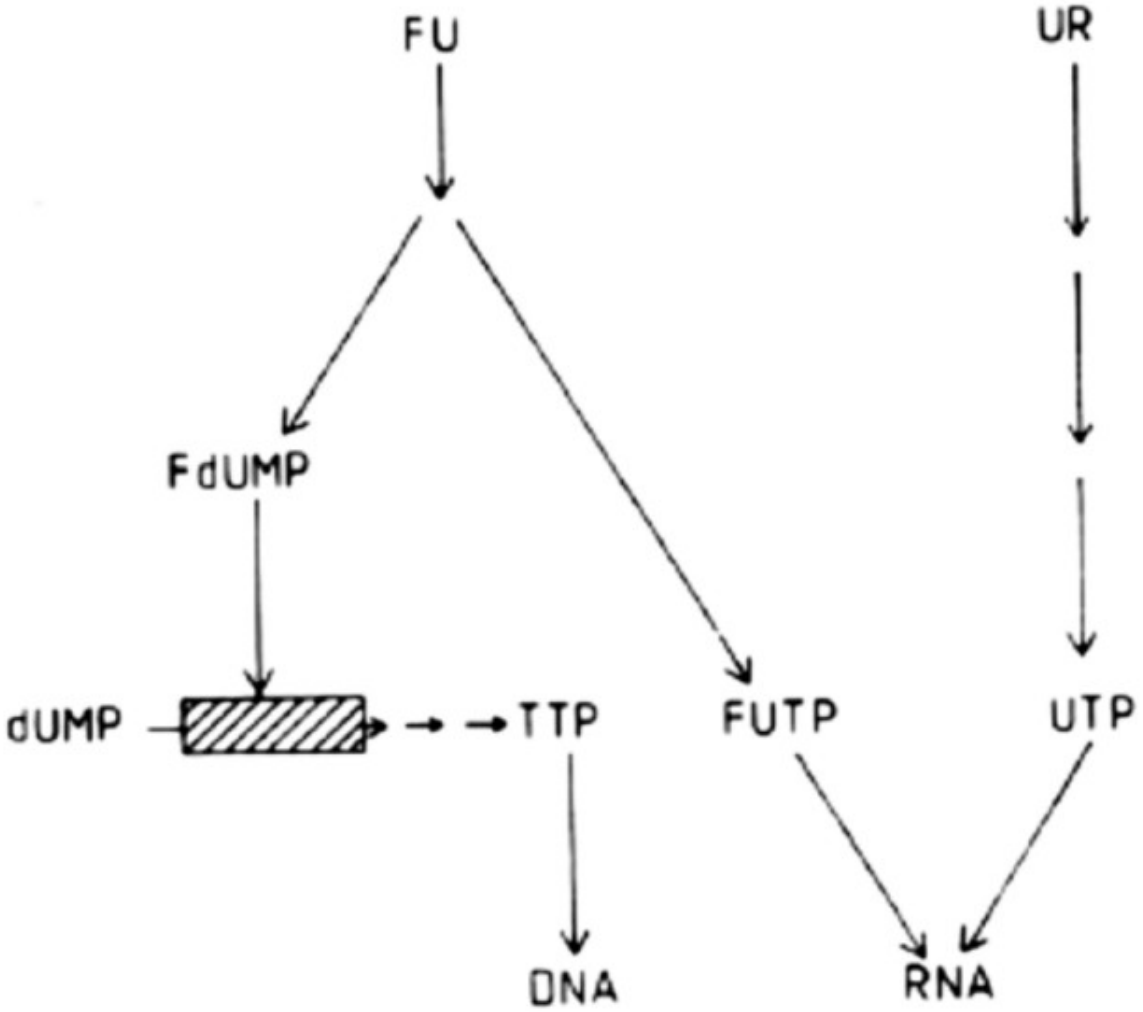


Uridine Triacetate (Vistogard):
Oral Prodrug
Course of therapy: $75,000
Drop shipped from Wellstat/BTG Pharmaceuticals

Activation pathway for 5-fluorouracil (5-FU):



Source: Brunton LL, Lazo JS, Parker KL: *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 11th Edition: http://www.accessmedicine.com


FU
UR
FdUMP
dUMP
TTP
FUTP
UTP
DNA
RNA

Uridine Triacetate (Vistogard):
Oral Prodrug
Course of therapy: $75,000
Drop shipped from Wellstat/BTG Pharmaceuticals

Some Cases for Consideration

55 year old male presents to the ED after a fall. He is awake and alert.
HR 110 bpm; BP 120/70 mmHg; RR 15/minute; 98% saturation RA

He has a tib-fib fracture and has to go to the OR

PMH: DVT x2; on dabigatran 150 mg twice daily

The ED is asking if Idarucimab should be administered before the OR?

What if there were endless resources and cost didn't matter?

Dart RC et al. Expert Consesus Guidelines for Stocking of Antidotes in Hospitals that Provide Emergency Care. Ann Emerg Med 2017

What if there were endless resources and cost didn't matter?

- Dantrolene
- Digoxin immune Fab
- Hydroxocobalamin
- Fomepizole
- Various Antivenoms
- DMSA/BAL
- Uridine Triacetate
- Glucarpidase

Dart RC et al. Expert Consesus Guidelines for Stocking of Antidotes in Hospitals that Provide Emergency Care. Ann Emerg Med 2017

Long Term Solutions

- Regional sharing of costly antidotes
- More rigorous pharmacoeconomic studies
- Poison Center's and Toxicologist an integral part of decision making process

Paying the Piper: Strategies for managing high cost antidotes

Background

Reasons

Pharmacoeconomics

Risks vs Benefits

Jeanna M. Marraffa, Pharm.D., DABAT, FAACT
Upstate New York Poison Center, Upstate Medical University
Syracuse NY

I have no financial disclosures to report