

Pearls #2: FD&C Blue Dye 2 and Sulfa Allergy

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Disclosures

- I have no financial interests relevant to the content of this presentation

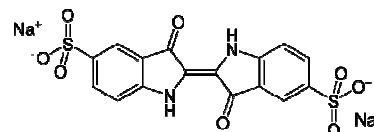
Case Study 1

- DK – 61 yowm with a multiyear history of hand dermatitis
- Explosive flare of dermatitis after change of dosage of Glyburide/Metformin mix.
 - Change from white tablets to “black” tablets
 - Resolved with switch back to old pills
- Black tablets colored with Indigo Carmine



Indigo Carmine Dye

- 5,5'-indigodisulfonic acid sodium salt, also known as indigotine or FD&C Blue #2
- Color in foods, medications, and used as an imaging agent in Urology, GYN, and GI



Indigo Carmine Allergy

- Indigo carmine – reports of anaphylaxis associated with use is cystoscopy
 - Seen in a patients with sulfa allergy
 - Gousse, et al -Urology 56(3): September 2000
 - Graziano et al – Int Urogynecol J, 16:418-419, 2005

Case Study 2

- LG 16 yowf with severe flare of long standing atopic eczema
 - Required concurrent Rx with daily prednisone 30 mg/day, azathioprine 225 mg/day, and CSA 300 mg/day, cetirizine 10 mg bid, zafirlukast 20 mg bid, and doxepin 50 mg qhs.
 - Remarked that she noted acute worsening of itch shortly after taking doxepin
 - Known allergy to sulfa – hives

Dailymed

At the present time this Web site does not contain a complete listing of labels for approved prescription drugs. Currently this Web site contains 231114 drugs.

About DailyMed
DailyMed provides high quality information about marketed drugs. This information includes FDA labels (package inserts). This Web site provides health information providers and the public with a standard, comprehensive, up-to-date, look-up and download resource of medication content and labeling as found in medication package inserts. The National Library of Medicine (NLM) provides this as a public service and does not accept advertisements.

Drug labeling and other information in the SPL is what has been most recently submitted by drug companies to the Food and Drug Administration (FDA) as drug listing information (see 21 CFR part 312). The drug labeling on this Web site may not be the labeling on currently distributed products or identical to the labeling that is approved. Drugs marked "OTC monograph final" or "OTC monograph not final" are not checked for conformance to the monograph. Drugs marked "unapproved" on this Web site have not been reviewed by FDA for safety and efficacy and their labeling has not been approved. For more information about unapproved drugs, visit <http://www.fda.gov/cder/otc/activities/otc.htm>.

Other information about drugs may also be available. NLM regularly processes data files uploaded from FDA's system and provides and maintains this Web site for the public to use in accessing the information. Additional information about medicines is available on NLM's MedlinePlus Web site <http://www.nlm.nih.gov/medlineplus>.

<http://dailymed.nlm.nih.gov/dailymed/about.cfm>

Search results for
DOXEPIN capsule (Sulfa Rx USA)

20 Results Found (Cover 20)

- Doxepin Hydrochloride (doxepin hydrochloride) Capsule (Mylan Pharmaceuticals Inc.)
- DOXEPIN HYDROCHLORIDE (doxepin hydrochloride) capsule (Watson Pharmaceuticals, Inc.)
- Doxepin Hydrochloride (doxepin hydrochloride) Capsule (Watson Laboratories, Inc.)
- DOXEPIN HYDROCHLORIDE capsule (Contract Pharmacy Services PA)
- DOXEPIN HYDROCHLORIDE capsule (Mid Health Pharma, LLC)

DOXEPIN capsule (Sulfa Rx USA)

Drug Label Sections
 HUMAN PRESCRIPTION DRUG LABEL | DEA Schedule | Marketing Status | Abbreviated New Drug Application

Drug Label Sections
 Description | Clinical Pharmacology | Indications & Usage | Contraindications | Warnings | Precautions | Adverse Reactions | Overdose | Dosage & Administration

Suicidality and Antidepressant Drugs
 Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of doxepin or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Doxepin is not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients and PRECAUTIONS: Pediatric Use.)

DESCRIPTION
 Doxepin hydrochloride is one of a class of psychotherapeutic agents known as tricyclic antidepressants. The molecular formula of the compound is C₁₈H₁₉NO and has a molecular weight of 275. It is a white crystalline solid readily soluble in water, lower alcohols and chloroform. It may be represented by the following structural formula:

C1=CC=C(C=C1)C2=CC=CC=C2N3C=CC=CC=C3

PRODUCT INFO
 Product Code: 0275-1048 | Dosage Form: CAPSULE
 Route of Administration: ORAL | DEA Schedule:

INGREDIENTS

Name (Active Moiety)	Type	Strength
Doxepin Hydrochloride (Doxepin)	Active	10 MILLIGRAM in 1 CAPSULE
black iron oxide	Inactive	
colloidal silicon dioxide	Inactive	
D&C Yellow No. 10 Aluminum Lake	Inactive	
gelatin	Inactive	
hydroxypropyl methylcellulose	Inactive	
hydroxypropyl starch	Inactive	
polyethylene glycol	Inactive	
SOLUSOLV	Inactive	
SD-40 alcohol	Inactive	
sulfonic black B	Inactive	
Titanium dioxide	Inactive	
FD&C Yellow No. 6 Aluminum Lake	Inactive	

APPEARANCE INFORMATION

Characteristic Appearance	Characteristic	Appearance
Color	WHITE (Capsule Body)	1
Shape	CAPSULE	Symbol
Imprint Code	MPL/LAN/1048	None
Size	None	None

LG Course

- Doxepin tablets/capsules D/C'd and liquid concentrate without dyes substituted.
- Blue 2 eliminated from foods
 - Breakfast cereals, yogurt, candy
- Prednisone and CSA stopped and AZA dose dropped to 150 mg/day
- Minimal dermatitis and itching persisted

Other excipients

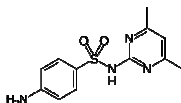
- Other FD&C and D&C dyes
 - Yellows #5, 6, & 10
 - Reds #28 & 40
 - Green #3
 - Blue #1
- Benzyl alcohol
- Parabens

Summary of Cases

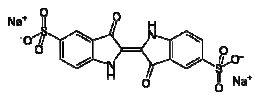
- 12 patients identified at TEC over past 18 months
- 8F/4M
- Generally presented with aggravation of pre-existing condition
- Sulfa allergy documented in 7/12
 - ASA allergy in 3 – appears to be cross reactivity with a variety of D&C and FD&C dyes

Summary of Cases

- Medications implicated
 - Doxepin
 - SSRI's
 - Multivitamins
 - HTN medications
- Beware of white tablets – bluing agents added for brightness – most often FD&C blue 1
- Daily Med a valuable resource
 - <http://dailymed.nlm.nih.gov/dailymed/about.cfm>



Sulfamethoxazole



Indigo Carmine

What is a drug and what is a dye?

- Many drugs we use are derived from chemical libraries derived from dye chemistry
- Why is it implausible to think that dyes can cause skin reactions when it is universally accepted that drug allergies have skin manifestations?