Disclosures

• Steve and Zach work for Rocky Mountain Health Plans.
• We do not have any financial interest in the medications we are discussing today.
• We have no intention to malign any person, business or product.
QUESTION 1

• Krystexxa, an IV infusion for treating gout, costs about...
  – A) $250 per month
  – B) $1 BILLION dollars per month
  – C) $7,500 per month
  – D) $65,000 per month
QUESTION 2

• Strep throat, like UTI, represents a good example of using a short course of antibiotics for good efficacy and safety
  – A) YES
  – B) NO
Zurampic (lesinurad)

- A new Z-drug!
- Approved in late 2016, Zurampic (lesinurad) is ADD-ON therapy for tx of gout
- Indication
  - Adjunctive treatment of gout-associated hyperuricemia in patients whose sUA level fails to reach goal with xanthine oxidase monotherapy
    - Must be used along with a xanthine oxidase inhibitor
      » Allopurinol, Uloric (febuxostat)
Zurampic (lesinurad)

- **MOA**
  - Uric acid transporter 1 (URAT1) inhibitor
    - Inhibits the function of transporter proteins involved in uric acid reabsorption in the kidney
    - URAT1 is responsible for the majority of the reabsorption of filtered uric acid from the proximal renal tubules
    - Also reduces thiazide related hyperuricemia by blocking organic anion transporter 4 (OAT4)
Zurampic (lesinurad)

• Efficacy
  – Three trials conducted, one published, two as a poster
  – CLEAR 1 (published), CLEAR 2 (poster)
    • Total of 1213 patients
    • sUA >6.5 mg/dL, ≥2 gout flairs in last 12 months despite allopurinol use
    • Patients got add on tx with lesinurad 200mg, 400mg, or placebo
    • Statistically significant reduction < 6mg/dL at 6 months
      – 28% vs. 54%, NNT = 4
      – But 400mg was no better and had more A/E
Zurampic (lesinurad)

- Efficacy
  - CRYSTAL, the third trial (poster)
    - Lesinurad vs. Uloric (febuxostat) in tophaceous gout
      - N=324
      - Lesinurad 200mg, 400mg, vs. febuxostat 80mg
    - Patients achieving sUA < 5mg/dL
      - 200mg (56.6%), 40mg (76.1%), placebo (46.8%)
        » 200mg reduction was not statistically significant at 6 months, but was by 12 months
  - In all three trials, there was no significant difference in the rate of gout flares, or in the rate of completion of at least 1 tophus, w/in 12 months
Zurampic (lesinurad)

• Safety
  – Increase in SCr occurred in 4.3% of patients in studies, 2.3% in patients on placebo + XOI. **NNH = 50**
  – Renal failure rates were not different from placebo (was numerically lower)
  – Nephrolithiasis was not different from placebo (was numerically lower)
  – **In monotherapy studies, lesinurad:**
    • resulted in SCr increases in 8.4% of patients, 0% in placebo group. **NNH = 12**
    • Resulted in renal failure in 9.3% of patients, 0% in placebo group. **NNH = 11**
    • Resulted in nephrolithiasis in 0.9% of patients, 0% in placebo group. **NNH = 111**
  – **Bottom line, lesinurad causes more renal related adverse events if not used along with a xanthine oxidase inhibitor**
Zurampic (lesinurad)

• Dosing
  – 200mg, once per day, with food and water
  – MUST be taken with allopurinol or febuxostat
  – Do not start in patients with GFR<45 mL/min
  – Take at least 2 liters of fluid per day while on tx
  – Assess renal function at baseline and periodically during therapy
    • Contraindicated if eGFR < 30 mL/min
  – Stop temporarily if SCr increases more than 2X

• Cost - ~ $350 per month
Zurampic (lesinurad)

- Other options
  - Optimize allopurinol dose
    - ~$8 to $46/month
  - Use the other uricosuric agent, probenecid
    - ~ $45 / month
  - Use Krystexxa (pegloticase) – intravenous
    - Urate oxidase enzyme, very effective
    - ~ $67,636 per month
Antibiotic length of therapy

• Rationale for using a longer course of therapy:
  – To prevent relapse and limit resistance
• But is there evidence to the contrary?
  – Longer courses may be more likely to cause resistance (via normal flora’s exposure)
  – Shorter courses work just as well for certain infections
• Example: uncomplicated cystitis is now very commonly 3 days of therapy, not 10
Antibiotic length of therapy

• Benefits of shorter course of therapy
  – Lessen the risk of resistance
  – Reduce adverse effects including superinfection
  – Reduce cost
  – Increase adherence
Antibiotic length of therapy

Antibiotics.mp4
Antibiotic length of therapy

• Acute bacterial sinusitis
  – IF antibiotics are necessary:
    • Adults, uncomplicated, 5-7 days
    • 5 days as effective as 10 for most adults
      – (Evidence level A; high quality meta-analysis]
    • 10-14 days may be necessary for complicated infections, or infections in children

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use
Antibiotic length of therapy

• Acute Exacerbations of Chronic Bronchitis
  — Likely no antibiotic needed
  — If suspected pneumonia:
    • ≤5 days if mild or moderate [Evidence Grade A]

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use
Antibiotic length of therapy

• Community acquired pneumonia
  – Five days of therapy is equally effective compared to longer durations, even in hospitalized CAP patients, with pneumonia severity index scores primarily ranging from I to IV, [Evidence level A; high-quality RCT]
  – Longer courses may be necessary in some patients (e.g., previous antibiotic treatment, immunosuppressed, requiring chest tube placement, mechanical ventilation, severe sepsis, pneumonia severity index score = V

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use
Antibiotic length of therapy

• Cellulitis
  – 5 days as effective as 10 for uncomplicated, if improvement is seen by 5 days
    • Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. *Arch Intern Med.* 2004 Aug 9-23;164(15):1669-74.

• Intra-abdominal infections
  – Four to five days if the infection source is controlled
    [Evidence level A high-quality RCT]
Antibiotic length of therapy

• Osteomyelitis
  – Infectious Diseases Society of America guidelines endorse six weeks of antibiotic therapy for vertebral osteomyelitis based on a recent study showing no difference between 6 and 12 weeks of therapy [Evidence level A; high-quality RCT].

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use.
Antibiotic length of therapy

• Acute OM
  – If antibiotics are deemed necessary:
    • AAP recommends 5 to 10 days
      – Children < 2 years old, 10 days
      – Older than 2 years old, 5 to 7 days, may consider 3 days with uncomplicated infection
        » [Evidence level A; high-quality meta-analysis]

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use.
Antibiotic length of therapy

• Pediatric UTI
  – 7 to 14 days
  – Older school age children w/o fever, consider 2 to 4 days
  – Avoid single dose therapy (reduced efficacy)

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use
Antibiotic length of therapy

- Adult uncomplicated UTI
  - SMX/TMP – 3 days
  - Nitrofurantoin – 5 days
- Stick with longer duration in pregnancy, complicated UTI, elderly

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use.
Antibiotic length of therapy

• Pyelonephritis
  – Uncomplicated, non-hospitalized patients:
    • Levofloxacin 750mg x 5 days (ciprofloxacin x 7 days)
    • SMX/TMP x 14 days
  – Consider fluoroquinolone x 7 days if hospitalized
    – Duration of antibiotic treatment for acute pyelonephritis and 
      septic urinary tract infection—7 days or less versus longer 
      treatment: systematic review and meta-analysis of 
      randomized controlled trials. *J Antimicrob Chemother* 

Refer to the Nov. 2016 issue of The Prescribers Letter for a 
complete list of meta analyses and citations that support these 
recommendations for antibiotic use
Antibiotic length of therapy

• Strep throat
  – Treat with appropriate antibiotic x 10 days to reduce risk of rheumatic fever

• Other conditions requiring longer course:
  – Active tuberculosis
  – Endocarditis
  – Osteomyelitis
  – Immunosuppressed patients
  – Those with recurrent infection
  – S/S of active infection

Refer to the Nov. 2016 issue of The Prescribers Letter for a complete list of meta analyses and citations that support these recommendations for antibiotic use
Flulaval has an advantage over Fluzone, the other quadrivalent vaccine approved down to 6 months of age: Flulaval dose is the same, regardless of age. Fluzone (manufactured by Sanofi Pasteur), is given as 0.25 mL for children 6-35 months, and 0.5mL for older patients, somewhat complicating the regimen.
Bevespi
(glycopyrrolate 9mcg + formoterol fumarate 4.8mcg)

• New anticholinergic + long-acting beta2-agonist. (LAMA/LABA)
  – Other LAMA/LABA inhalers:
    • Stiolto, Anoro Ellipta

• Indication:
  – Long-term maintenance treatment of airflow obstruction in COPD, including chronic bronchitis and/or emphysema
  – **NOT** for relief of acute bronchospasm or treatment of asthma

• Manufactured by AstraZenaca
Bevespi

• Mechanism of Action
  – Glycopyrrolate
    • LAMA – long-acting anti-muscarinic agent (anticholinergic) that inhibits the muscarinic receptor M3 in the smooth muscle in the airways, resulting in bronchodilation
  – Formoterol fumarate
    • LABA – long-acting selective beta2-adrenergic agonist that stimulates the production of cAMP and rapidly causes relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells.
Bevespi
(glycopyrrolate 9mcg + formoterol fumarate 4.8mcg)

• Dosing
  – Inhale 2 puffs by mouth twice daily
    • This is also MAX dosing
    • 18 years of age and older
  – Meter Dose Inhaler (MDI)
    • 10.7 g inhaler size
    • 120 puffs/inhaler

• Contraindication
  – LABA use in asthma patients without use of long-term control medication

• Still prescribe SABA for acute control
Bevespi
(glycopyrrolate 9mcg + formoterol fumarate 4.8mcg)

• Efficacy
  – 2 placebo-controlled trials
  – 8 dose-ranging trials

• Trial 1 and Trail 2
  – 24 week, n= 3,699, randomized, placebo-controlled, double-blind study in patients with moderate to very severe COPD
  – Inclusion criteria:
    • 40 – 80 years of age, history of smoking ≥ 10 pack per years, post-albuterol FEV$_1$ < 80% predicted, and FEV$_1$/FVC < 0.7.
Bevespi
(glycopyrrolate 9mcg + formoterol fumarate 4.8mcg)

– Demographics:
  • 56% males, 91% Caucasian, mean age of 63, 54% current smokers with avg. of 51 pack-year, mean percent predicted post-albuterol was 51% (19% - 82%)

– Primary endpoint:
  • Change from baseline FEV₁ at 24 weeks with Bevespi compared to placebo, glycopyrrolate only, formoterol only.
Bevespi
(glycopyrrolate 9mcg + formoterol fumarate 4.8mcg)

– Results:
  • Shows larger increase in mean change in trough FEV₁ from baseline compared to placebo, glycopyrrolate, or formoterol fumarate
  • Trial 1
    – Mean peak FEV₁ improvement from baseline vs. placebo at week 24 was 291mL (252-331)
    – FEV₁ mean increase 5 minutes after first dose was 187mL (168-205)
  • Trial 2
    – Mean peak FEV₁ improvement from baseline vs. placebo at week 24 was 267mL (226-308)
    – FEV₁ mean increase 5 minutes after first dose was 186mL (164-207)
Bevespi

Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]

Group C

LAMA + LABA

LABA + ICS

Further exacerbation(s)

LAMA

Group D

Consider roflumilast if FEV₁ < 50% pred. and patient has chronic bronchitis

Consider macrolide (in former smokers)

Further exacerbation(s)

LAMA + LABA + ICS

LAMA + LABA

LABA + ICS

Persistent symptoms/further exacerbation(s)

LAMA

Group A

Continue, stop or try alternative class of bronchodilator

evaluate effect

A bronchodilator

Preferred treatment

In patients with a major discrepancy between the perceived level of symptoms and severity of airflow limitation, further evaluation is warranted.
FDA changing how pregnancy/lactation/reproductive information is presented in a package insert

Pregnancy an Lactation labeling (drugs) final rule – 12/03/2014

Updates to package insert will occur:
1. For any new prescription drug or biologic product approval after June 30, 2015
2. Anytime a previously approved drug updates the package insert for any reason or within 3 years of the final rule

Labeling for OTC medications will not be affected by this rule and therefore not change
Pregnancy/Lactation Data

Pregnancy + Labor and Delivery ➔ Pregnancy

The Pregnancy subsection (8.1) includes information for a pregnancy exposure registry for the drug when one is available. Pregnancy exposure registries collect and maintain data on the effects of approved drugs that are prescribed to and used by pregnant women. Information about the existence of any pregnancy registries in drug labeling has been recommended but not required until now. Information in the Pregnancy sub-section includes a Risk Summary, Clinical considerations, and Data. Information formerly found in the “Labor and delivery” subsection is now included in the “Pregnancy” subsection.

Nursing Mothers ➔ Lactation

The Nursing mothers subsection was renamed, the Lactation subsection (8.2), and provides information about using the drug while breastfeeding, such as the amount of drug in breast milk and potential effects on the breastfed infant.

New Category ➔ Female and Males of Reproductive Potential

The Females and Males of Reproductive Potential subsection (8.3), new to the labeling, includes information, when necessary, about the need for pregnancy testing, contraception recommendations, and information about infertility as it relates to the drug.
Pregnancy/Lactation Data

Old

8.1. Pregnancy

Teratogenic Effects:

Pregnancy Category C. There are no adequate and well-controlled trials of BEVESPI AEROSPHERE or its individual components, glycopyrrolate and formoterol fumarate, in pregnant women. Because animal reproduction studies are not always predictive of human response, BEVESPI AEROSPHERE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women should be advised to contact their physicians if they become pregnant while taking BEVESPI AEROSPHERE.

Glycopyrrolate: There was no evidence of teratogenic effects in rats and rabbits at approximately 18,000 and 270 times, respectively, the maximum recommended human daily inhalation dose (MRHIDD) in adults (in mg/m² basis at a maternal oral dose of 65 mg/kg/day in rats and at a maternal intramuscular injection dose of 0.5 mg/kg in rabbits).

Single-dose studies in humans found that very small amounts of glycopyrrolate passed the placental barrier.

Formoterol Fumarate: Formoterol fumarate has been shown to be teratogenic, embryocidal, to increase pup loss at birth and during lactation, and to decrease pup weights in rats and teratogenic in rabbits. These effects were observed at approximately 1,500 (rats) and 61,000 (rabbits) times the MRHID (on a mg/m² basis at maternal oral doses of 3 mg/kg/day and above in rats and 60 mg/kg/day in rabbits). Umbilical hernia was observed in rat fetuses at approximately 1,500 times the MRHID (on a mg/m² basis at maternal oral doses of 5 mg/kg/day and above). Prolonged pregnancy and fetal brachygnathia was observed in rats at approximately 7,900 times the MRHID (on a mg/m² basis at an oral maternal dose of 15 mg/kg/day in rats). In another study in rats, no teratogenic effects were seen at approximately 600 times the MRHID (on a mg/m² basis at maternal inhalation doses up to 1.2 mg/kg/day in rats).

Subcapsular cysts on the liver were observed in rabbit fetuses at an oral dose approximately 61,000 times the MRHID (on a mg/m² basis at a maternal oral dose of 60 mg/kg/day in rabbits). No teratogenic effects were observed at approximately 3,600 times the MRHID (on a mg/m² basis at maternal oral doses up to 3.5 mg/kg day).

8.2. Labor and Delivery

There are no well-controlled human trials that have investigated the effects of BEVESPI AEROSPHERE on preterm labor or labor at term. Because beta-agonists may potentially interfere with uterine contractility, BEVESPI AEROSPHERE should be used during labor only if the potential benefit justifies the potential risk.

8.3. Nursing Mothers

It is not known whether BEVESPI AEROSPHERE is excreted in human milk. Because many drugs are excreted in human milk and because formoterol fumarate, one of the active ingredients in BEVESPI AEROSPHERE, has been detected in the milk of lactating rats, caution should be exercised when BEVESPI AEROSPHERE is administered to a nursing woman. Since there are no data from controlled trials on the use of BEVESPI AEROSPHERE by nursing mothers, a decision should be made whether to discontinue nursing or to discontinue BEVESPI AEROSPHERE, taking into account the importance of BEVESPI AEROSPHERE to the mother.

New

8.1. Pregnancy

Risk Summary:

There are no randomized clinical studies of AIRDUO RESPICLICK or individual monopropionate fluticasone propionate and salmeterol xinafoate, in pregnant women. There are clinical considerations with the use of AIRDUO RESPICLICK in pregnant women (see Clinical Considerations). Animal reproduction studies are available with the combination of fluticasone propionate and salmeterol xinafoate as well as individual monopropionate. In animals, teratogenicity characteristic of corticosteroids, decreased fetal body weight and/or skeletal variations, in rats, mice, and rabbits were observed with subcutaneously administered maternal toxic doses of fluticasone propionate less than the maximum recommended human daily inhalation dose (MRHID) on a mg/m² basis [see Data]. However, fluticasone propionate administered via inhalation to rats decreased fetal body weight, but did not induce teratogenicity at a maternal toxic dose less than the MRHID on a mg/m² basis [see Data]. Experience with oral corticosteroids suggests that rodents are more prone to teratogenic effects from corticosteroids than humans. Oral administration of salmeterol to pregnant rabbits caused teratogenic characteristic of beta-adrenoceptor stimulation at maternal doses approximately 700 times the MRHID on a mg/m² basis. These adverse effects generally occurred at large multiples of the MRHID when salmeterol was administered by the oral route to achieve high systemic exposures. No such effects occurred at an oral salmeterol dose approximately 420 times the MRHID (see Data).

The estimated risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

In women with poorly or moderately controlled asthma, there is an increased risk of several perinatal adverse outcomes such as preclampsia in the mother and prematernity, low birth weight, and small for gestational age in the neonate. Pregnant women with asthma should be closely monitored and medication adjusted as necessary to maintain optimal asthma control.

Data

Fluticasone Propionate and Salmeterol: In an embryo/fetal development study with pregnant rats that received the combination of subcutaneous administration of fluticasone propionate and oral administration of salmeterol at doses of 0, 100, 300, 1000, 3010, 30,100, and 1000-10,000 mcg/m²/day (as fluticasone propionate/salmeterol) during the period of organogenese, findings were generally consistent with the individual monopropionate and there was no exacerbation of expected fetal effects. Omphalocele, increased embryo/fetal deaths, decreased body weight, and skeletal variations were observed in rat fetuses, in the presence of maternal toxicity, when combining fluticasone propionate at a dose approximately 2 times the MRHID (on a mg/m² basis at a maternal subcutaneous dose of 100 mcg/kg/day) and a dose of salmeterol at
Xtampza (oxycodone ER)

• The latest abuse deterrent opioid to hit the market

• Sixth ADO approved by FDA, preceded by:
  – Oxycontin (oxycodone ER)
  – Embeda (morphine sulfate ER)
  – Hysingla (hydrocodone ER) – not yet on market
  – Zohydro ER (hydrocodone ER)
  – Targiniq ER (oxycodone ER) – not yet on market

• Indication: moderate to severe pain in patients needing around the clock opioid therapy
Xtampza (oxycodone ER)

• Dosing
  – 9mg to 36mg BID
  – Max daily dose is 288mg (320mg oxycodone equivalent)
    • Has a max dose due to unknown effect on human safety of swallowing too much of the wax used as a deterrent
  – High fat meals increase plasma concentrations by 100% to 150%
  – Xtampza is the oxycodone base, dosing must be converted to equivalent oxycodone HCl to assess oxycodone and morphine equivalent dosing
Xtampza (oxycodone ER)

• Abuse deterrence
  – Uses the FDA defined “physical/chemical barrier” method
    • Fatty acids and waxes create microspheres that resist manipulation to inject or snort
    • Capsules can still be opened and sprinkled on food

• Cost
  – $450 to $1,250/month
    • (Similar to Oxycontin, Embeda, Zohydro)
Xtampza (oxycodone ER)

• Studies
  – Oral abuse deterrence study
    • R, DB, AC, PC, single dose, 6 way crossover. N=61
    • 38 completed the study
    • Treatment arms: Intact Xtampza 36mg fed and fasted
    • Xtampza 36mg chewed, fed and fasted
    • Oxycodone IR 40mg crushed in water
    • Placebo (boring!)
  – Outcome measures
    • Drug liking on 100 point VAS
    • Would do this again! On 100 point VAS
Xtampza (oxycodone ER)

• Results
  – Drug liking
    • Intact and chewed Xtampza, in fasted state, was less likeable than Oxy IR
      – This makes sense, knowing that the drug is less well absorbed in the fasted state, and you are comparing an ER drug to an immediate release drug professionally compounded up in water
    • Would do this again?
      – Intact and chewed Xtampza in fasted state was not different than Oxy IR
Xtampza (oxycodone ER)

• Nasal abuse study
  – R, DB, AC, PC, single dose, 4 way crossover. N=39
  – Xtampza 36mg, crushed given intranasally
  – Xtampza 36mg intact given orally
  – Oxy IR 40mg crushed given intranasally
  – Placebo (*boring!*)
  – Outcomes measures:
    • Drug liking, and “let’s do this again”, on 100 point VAS
  – Results:
    • Crushed intranasal Xtampza was statistically less likeable than Oxy IR
Xtampza (oxycodone ER)

• Summary
  – Remember that the most common route of abuse is intact oral, and abuse deterrent opioids do not have any effect
  – Injecting these drugs is more dangerous than injecting a “regular” opioid due to the composition of the drug
  – “Abuse deterrent” may cause a false sense of security for prescribers
  – Significant variation in plasma concentration depending upon fed state
  – No data yet exists on whether any abuse deterrent opioid reduces abuse. FDA investigating.
QUESTION 3

• Krystexxa, an IV infusion for treating gout, costs about...
  – A) $250 per month
  – B) $1 BILLION dollars per month
  – C) $7,500 per month
  – D) $65,000 per month
QUESTION 4

• Strep throat, like UTI, represents a good example of using a short course of antibiotics for good efficacy and safety
  – A) YES
  – B) NO
QUESTION 5

• Which is true about abuse deterrent opioids?
  – A) although more expensive than other opioids, the evidence shows reduced abuse and heroin use in the community
  – B) these drugs cannot be injected or snorted, making them a safer alternative than regular opioids
Tamper Resistant Requirements

8.800.11.D. TAMPER-RESISTANT PRESCRIPTION DRUG PADS OR PAPER

1. The use of tamper-resistant prescription drug pads or paper is required for all written or electronically printed prescriptions for all Medical Assistance Program clients when:

   a. Prescriptions are issued for outpatient drugs, including controlled and uncontrolled substances, or OTC drugs that are reimbursable through the Medical Assistance Program and dispensed by a pharmacy; and

   b. The Medical Assistance Program is the primary or secondary payer of the prescription being filled.

2. To be considered tamper-resistant, the pad/paper used for a written or electronically printed prescription shall integrate three distinct characteristics. The three characteristics and the specific features required are as follows:
Tamper Resistant Requirements

a. Characteristic #1: One or more industry-recognized features designed to prevent unauthorized copying of completed or blank prescription form. A prescription shall contain at least one of the following features:

i) Void/Illlegal/Copy Pantograph with or without the Reverse Rx feature. The word “Void”, “Illegal”, or “Copy” appears when the prescription is photocopied. If the paper has the Reverse Rx feature, the Rx symbol must disappear when photocopied at light setting. The Reverse Rx feature is not allowed as a feature by itself.

ii) Micro-fine printed security message generated by a computer, electronic medical records system or other electronic means. The message may serve as a signature line or border. This must be printed in 0.5 font or smaller and readable when viewed at 5x magnification or greater and illegible when copied.

iii) Coin-reactive ink or security mark. The pad or paper identifies an area on the pad/paper where the ink changes color or reveals wording or a picture when that area is rubbed by a coin. This must be accompanied by a message describing what is necessary to demonstrate authenticity.

iv) Security print watermark. Specific wording is printed on the front or back of the prescription paper and can only be seen when viewed at an angle.

v) Paper with a watermark. This is paper that contains a watermark that can be seen when backlit.
Tamper Resistant Requirements

b. Characteristic #2: One or more industry recognized features designed to prevent the erasure or modification of information written on the prescription by the prescriber. A prescription shall contain at least one of the following features:

i) An erasure-revealing background. This is a background that consists of a non-white solid color or consistent pattern that has been printed onto the paper. If an erasure or modification is attempted, the background will show marks or the color of the underlying paper where the alterations were made.

ii) Toner fusing technology for laser-printed prescriptions. This is a treatment that is added to the surface of the paper to create a strong bond between the laser-printed text and the paper. The computer-printed information cannot be lifted from the surface of the paper without damaging the paper.

iii) Chemical-reactive paper. This is paper that contains features that show discoloration or reveals a hidden message if solvents are used to attempt to wash the ink from its surface.

iv) Plain bond paper combined with inkjet-printing. The inkjet printing is absorbed into the high grade paper stock. Erasures and modifications cannot be made without damaging the paper.

v) Pre-printed quantity check-off boxes indicated in ranges of no more than 25 per range combined with a written quantity. The range box corresponding to the quantity prescribed must be checked by the prescriber for the prescription to be valid.

vi) Pre-printed refill indicator where the number of refills allowed is marked or no refills or “NR” is marked when no refills are authorized. Refill information must be completed by the prescriber for the prescription to be valid.

vii) Characters surrounding the authorized dispensing quantity and the number of refills. Special characters such as a series of asterisks must be repeated on both sides of the numbers indicating the quantity and the number of refills authorized (e.g., Quantity ***50*** Refill ***3***). This is acceptable only for prescriptions that are generated by a computer, electronic medical records system or other electronic means.
Tamper Resistant Requirements

c. Characteristic #3: One or more industry recognized features designed to prevent the use of counterfeit forms. A prescription must contain at least one of the following features:

i) Security features listed visibly in a box, band or border on the prescription. This must be a complete listing of all of the security features incorporated into the prescription pad/paper in order to minimize tampering.

ii) Security threads. Metal, fluorescent or plastic security threads are embedded into the prescription pad/paper.

iii) Thermochromic ink. All or some of the pad or paper is pre-printed with ink that changes color when exposed to heat and then changes back to its original color when cooled. This must be accompanied by a message describing what is necessary to demonstrate authenticity.