

## Ketek (Telithromycin)

- 2001 FDA advisory committee denied approval due to concerns about hepatotoxicity
- 2001 Sanofi conducts large trial to disprove hepatotoxicity concern
- 2003 Approved in Canada
- 2004 (April) Approved in USA (later to find out some data was fraudulent)



## Ketek (Telithromycin)

- 2006 (January) FDA announces Annals of Internal Medicine article describes 3 cases of liver toxicity
- 2006 Sanofi Aventis stops trials in Infants and Children
- 2006 (June 29) FDA issued “Public Health Advisory”
  - 12 cases of acute liver failure – 4 deaths/1 transplant
  - 23 cases of serious liver injury (more reported since)

<http://www.fda.gov/cder/drug/advisory/telithromycin.htm>



## Why is Ketek still on the market?

- FDA has concluded that the drugs' benefit to patients for the approved indications outweighs its risk, including the rare risk of liver failure

<http://www.fda.gov/cder/drug/infopage/telithromycin/default.htm>



## Why is Ketek still on the market?

- US Advisors suggest to limit it's use to treatment of pneumonia
  - Multi-drug resistant *Streptococcus pneumoniae* includes penicillin-resistant *Streptococcus pneumoniae* or isolates resistant to two or more of the following antibiotics: penicillin, 2nd generation cephalosporins, macrolides, tetracyclines and trimethoprim/sulfamethoxazole.

<http://www.fda.gov/cder/drug/infopage/telithromycin/default.htm>



## Quinine

- Since 1969, FDA has received 665 reports of adverse events with serious outcomes associated with quinine use, including 93 deaths
- 1995: FDA bans OTC Quinine



## Quinine

- 2006 (December)
  - FDA cautions consumers about risks of Quinine
  - FDA orders firms to stop making unapproved products
  - FDA will also crack down on “natural” Quinine (i.e. Cinchona)

<http://www.fda.gov/bbs/topics/NEWS/2006/NEW01521.html>



## Quinine

- *Qualaquin 324 mg* is the only FDA-approved quinine product on the market (\$4.38 per dose)
- The package insert for *Qualaquin* specifically says NOT to use quinine for leg cramps
- The FDA discourages use of quinine for leg cramps due to its unfavorable risk-to-benefit ratio



## Quinine

- Manufacturers of other quinine products, will have to quit making their products by February 2007, stop shipping by June 2007
- RGH will have Qualaquin available for use only with Infectious Disease approval



## Monitoring Quinine

- Monitor CBC with platelet count, liver function tests, blood glucose, ophthalmologic examination
  - Thrombocytopenia (onset often 7 days, not dose related)
  - Hepatitis (usually within first 2 months, not dose related)
  - Hypoglycemia – Quinine stimulates insulin release
  - Tinnitus, hearing impairment (with low dose)
  - Night blindness and/or optic atrophy
  - Cardiovascular (Angina, Torsades de Pointes)
  - Phototoxicity



## Alternatives to Quinine

- Consider trial off Quinine if someone has been on it long term\*

Managing nocturnal leg cramps – calf-stretching exercises and cessation of quinine treatment: a factorial randomised controlled trial

Coppin RJ; Wicke DM; Little PS SO Br J Gen Pract 2005 Mar;55(512):186-91



## Alternatives to Quinine

- Advise patient to be less sedentary
  - Using stationary bike for a few minutes before bedtime (especially for sedentary people)
- Using a heating pad on muscles before bed
- Loosen the covers in bed – prevent toes from pointing downward
- Assure appropriate calcium intake



## Alternatives to Quinine

- Reduce sugar and caffeine intake (decrease absorption of vitamins)
- Patient with flat feet or working on concrete all day, assure proper footwear
- Adequate fluid intake (especially elderly)
- Tonic Water: hydration / placebo effect?  
8 oz. of tonic water  $\approx$  20 mg of Quinine
- See internet for Patient Handout

[http://www.pharmacistsletter.com/\(S\(qtr3az55ukmi0qnltyt5pc145\)\)/pl/detaildocuments/230101.pdf?cs=&s=PL](http://www.pharmacistsletter.com/(S(qtr3az55ukmi0qnltyt5pc145))/pl/detaildocuments/230101.pdf?cs=&s=PL)

