FDA response to Codeine citizen’s petition

Suggested changes

Codeine should not be used to treat pain or cough in children younger than 12 years with the following exception: Outside the setting of post-tonsillectomy or adenoidectomy, codeine may be prescribed for pain management in children younger than 12 years old who are **known CYP2D6 normal metabolizers (NMs) or CYP2D6 intermediate metabolizers (IMs)** based on pharmacogenetic testing that includes *CYP2D6* copy number or gene duplication detection.

Our argument:

The Petition sets forth the following arguments in support of its request:

(1)"Pharmacogenetic testing can identify which patients may safely receive and benefit from codeine";

(2)"Alternative opioid analgesics also present risks to pediatric patients";

(3)"*CYP2D6* testing is available by Clinical Laboratory Improvement Amendments (CLIA)-accredited laboratories";

(4)"Pre-emptive *CYP2D6* testing has already been shown to inform the safe and effective use of codeine to treat pediatric pain, including in children under the age of 12";

(5)"Codeine in combination with acetaminophen is currently the only Drug Enforcement Administration (DEA) Schedule III opioid analgesic, which allows refills and verbal prescriptions"; and

(6)"Codeine is an important analgesic for pediatric patients with acute and chronic pain, including those with sickle cell disease."

FDA response:

- Substantial Risks to Patients Under Age 12 Remain, Even with *CYP2D6* Testing
  - Testing Variability
  - Imprecise Genotype-Phenotype Correlation
  - Inconsistent Test Access and Clinician Experience
  - Safety Concerns Beyond CYP2D6 Phenotype
    - Needs expert interpretation
    - UGT2B7
    - Cited other comorbidities that might cause respiratory depression
- Codeine's Role in the Treatment of Pediatric Pain
- Prescriber Convenience and Patient Access
  - Over the past few years – and particularly during the COVID-19 public health emergency – electronic prescribing is now permitted for Schedule II drugs, and the use of telemedicine is increasing
- The Existing Contraindication Continues to Reflect Agency Views