Implementation of CPIC Guidelines into Clinical Practice

Cleveland Clinic Experience
• 10 adult hospitals & a children’s hospital in Ohio
• Hospital in Florida
• Over 90 ambulatory locations in Ohio and Florida
• 5.5 million patient visits per year
Schematic of Pharmacogenomic Implementation
Oversight and Review

Pharmacogenomics Advisory Board
Center for Clinical Genomics

Personalized Medication Program
(Select Gene-Drug Pairs for Integration and Manage Workgroups)

Gene-Drug Pharmacogenomic Workgroups
(Develop Clinical Workflows and Decision Support Language)

Pharmacy & Therapeutics Committee
Informatics Physician Advisory Groups
(Inpatient, Ambulatory, Emergency)

Cleveland Clinic
Implementation Science
Gene-Drug Pairs Integrated into EHR

*TPMT* – thiopurines
Predictive of severe life-threatening myelosuppression

*HLA-B*57:01 – abacavir
FDA boxed warning. Predictive of serious and sometimes fatal hypersensitivity reaction

*HLA-B*15:02 – anticonvulsants
FDA boxed warning. Predictive of Stevens-Johnson syndrome/epidermal necrolysis

*G6PD* – oral dapsone
Predictive of acute hemolytic anemia
Clinical Decision Support for Guiding PGX Testing

• Cleveland Clinic does not have a preemptive genotyping protocol

• For gene-drug pairs selected for implementation, point-of-care reminders needed

• Interruptive pre-test alerts were deployed to the EHR that reminded (educate) clinicians to consider genetic testing
Example of Pharmacogenomic CDS

**HLA-B*57:01 – Abacavir**

- **FDA BLACK BOX WARNING:** RISK OF A SERIOUS FATAL HYPERSENSITIVITY REACTION. A HLA-B*57:01 genotype test is recommended before prescribing abacavir or reinitiating abacavir therapy, including for those who previously tolerated abacavir therapy. Please click 'accept' below to order the HLA-B*57:01 genotype test or a reason for not ordering the test.

- **External result noted by clinician**

- **Used to identify those with PGx tests from outside health systems**
Example of Pharmacogenomic CDS

**HLA-B*15:02 – Carbamazepine**

Selection of these acknowledgements suppresses future pre-test alerts to prevent alert fatigue
RISK OF A SERIOUS/ FATAL DERMATOLOGIC REACTION: The patient is positive for the HLA-B*15:02 allele and is at an increased risk of a serious/fatal dermatologic reaction to the following antiepileptic medications:

- carbamazepine
- oxcarbazepine
- eslicarbazepine
- phenytoin
- fosphenytoin
- lamotrigine

These medications should NOT be prescribed unless the benefit outweighs the risk, or if the patient has consistently been

CLEVELAND CLINIC PERSONALIZED MEDICATION PROGRAM

HLA-B*15:02 – ANTICONVULSANTS CONSENSUS GUIDELINES

PURPOSE OF DOCUMENT: Individuals who carry the HLA-B*15:02 allele are approximately 100-fold more susceptible to carbamazepine-induced Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) than those who are non-carriers of the allele. Although this document focuses on carbamazepine, carriers of the HLA-B*15:02 allele may also be more susceptible to oxcarbazepine, eslicarbazepine acetate, phenytoin, fosphenytoin, and lamotrigine-induced SJS/TEN than non-carriers. HLA-B genotyping is offered at Cleveland Clinic (test name HLA B*1502) to help identify those at an increased risk of drug-induced SJS/TEN. The purpose of this document is to provide guidance for when this test should be ordered, how to interpret the result, and how to modify pharmacotherapy based on the HLA-B*15:02 test result.

Evidence-based referenced education documents linked to decision support for CMS Stage 2 meaningful use criteria
Pharmacogenomic Decision Support
Clinical Resources

Stored in a Microsoft SharePoint® site that interfaces with the EHR
Entry of *HLA* results (negative/positive) is an automated process.
Entry of *TPMT* results into discrete data field requires manual annotation
**HLA-B*15:02 – Carbamazepine**

Patient Safety Alerts

*RISK OF A SERIOUS/FATAL DERMATOLOGIC REACTION:* The patient is positive for the HLA-B*15:02 allele and is at an increased risk of a serious/fatal dermatologic reaction to the following antiepileptic medications:

- carbamazepine
- oxcarbazepine
- eslicarbazepine
- phenytoin
- fosphenytoin
- lamotrigine

These medications should NOT be prescribed unless the benefit outweighs the risk, or if the patient has consistently been taking the medication for greater than 3 months without a cutaneous reaction. Please cancel this drug order and prescribe an alternate drug, or select a reason for ordering.

Please page the pharmacogenomics pharmacist at 22924 for more information.

Click here for additional information about HLA*B15:02 - Anticonvulsants

Last HB1502=Positive on 8/12/2015

Acknowledge reason:

- Med Update
- Consistently taking drug > 3 months
- Benefit Outweighs Risk
- Emergency
- Other - Document in note

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Cleveland Clinic
CDS Formative Evaluation

Alert Language Easy to Understand

Practice Recommendations: Involve clinicians early

n=38

Cleveland Clinic
CDS Formative Evaluation

Alert Does Not Impact Workflow

Practice Recommendations: Involve clinicians early
Passive Clinical Decision Support for Guiding PGX

• Reserve interruptive PGx alerts for very high-risk gene-drug

• Passive decision support for other gene-drug interactions
  – Reduce alert fatigue
  – Faster integration of PGx data into EHR

• PGx data initially resulted in the EHR is textual
  – Not sustainable to manually annotate results
Pharmacogenomic Test Reporting in Drug Entry Screen

**Carbamazepine 200 mg tab(s) (TEGretol)**
200 mg, ORAL, 2 TIMES DAILY, First Dose Today at 2100, Until Discontinued

<table>
<thead>
<tr>
<th>Component</th>
<th>Time Elapsed</th>
<th>Value</th>
<th>Range</th>
<th>Status</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA B*1502 Typing</td>
<td>506 days (03/05/14 0700)</td>
<td>POSITIVE (NOTE) The allele HLA-B*1502 is associated with increased risk of developing severe skin reactions to carbamazepine therapy (Stevens-Johnson Syndrome and toxic epidermal necrolysis).</td>
<td></td>
<td>Final result</td>
<td></td>
</tr>
</tbody>
</table>

**Reference Links:**
1. HLA-B*1502 Pharmacogenomic Summary Sheet
2. Drug Info - Adult
3. Drug Info - Peds

**Dose:**
- 200 mg
- 200 mg
- 400 mg
- 600 mg

**Administer Dose:** 200 mg
**Administer Amount:** 1 tablet

**Route:** ORAL

**Frequency:** 2 TIMES DAILY

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Pharmacogenomic Test Reporting in Drug Entry Screen

<table>
<thead>
<tr>
<th>Component</th>
<th>Time Elapsed</th>
<th>Value</th>
<th>Range Status</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPMT Enzyme</td>
<td>202 days (01/06/15 1453)</td>
<td>22.4 Unit U/mL RBC (NOTE) This result can be interpreted as normal for TPMT activity.</td>
<td>Final result</td>
<td></td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Dose:</th>
<th>ORAL</th>
<th>50 mg</th>
<th>100 mg</th>
<th>150 mg</th>
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</thead>
<tbody>
<tr>
<td>Route:</td>
<td>ORAL</td>
<td>DAILY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For:</td>
<td>Doses</td>
<td>Hours</td>
<td>Days</td>
<td></td>
</tr>
<tr>
<td>Starting:</td>
<td>7/28/2015</td>
<td>Today</td>
<td>Tomorrow</td>
<td></td>
</tr>
<tr>
<td>First Dose:</td>
<td></td>
<td>Include Now</td>
<td>As Scheduled</td>
<td></td>
</tr>
<tr>
<td>First Dose:</td>
<td>Today 1200</td>
<td>Until Discontinued</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Pharmacogenomic Decision Support
Impact on Patient Care

• Compliance with clinical recommendations
  – Contraindications – 100% compliant
  – Dose reductions – 90 to 95% compliant
Pharmacy Managed Behind-The-Scenes Review of Pharmacogenomic Test Ordering & Results

EHR In Basket – Pharmacy View

- Provides a summary of PGx Enterprise wide
- Review for correct test selection – Cost Savings
- Follow up with clinicians when necessary
### Personalized Medication Program
**EHR Pharmacogenomic Consult Request**

**Consult Clinical Pharmacogenomics**

Routine, ONCE First occurrence Today at 1545, For emergent questions, contact the pharmacogenomics clinical pharmacist at pager 22924.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Prompt</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Is the consult for clinical interpretation and drug dosing recommendations for a pharmacogenomic test result?</td>
<td>Yes, indicate which test result and which drug</td>
</tr>
<tr>
<td>2.</td>
<td>Is the consult for an opinion on whether pharmacogenomics may help explain drug intolerances?</td>
<td>Yes, indicate which drug(s) and the observed adverse drug effect</td>
</tr>
<tr>
<td>3.</td>
<td>Is the consult for an opinion on whether pharmacogenomics may help explain non-response to a drug?</td>
<td>Yes, indicate which drug(s)</td>
</tr>
<tr>
<td>4.</td>
<td>What other information is being requested (if applicable)?</td>
<td></td>
</tr>
</tbody>
</table>

**Priority:** Routine
**Frequency:** ONCE
Cleveland Clinic's MyConsult® Online Medical Second Opinion now offers a consultation service for individuals who are seeking an expert second opinion regarding pharmacogenomics.
Implementation of Pharmacogenomic Services

• Outpatient Pharmacogenomics Clinic

Genomic Medicine Institute

The Center for Personalized Genetic Healthcare
Your family history is your road map to wellness. Treatment is centered around your unique genetic profile, and its impact on you and your family.

Dr. Charis Eng
Chair, Genomic Medicine Institute

Cleveland Clinic
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Every life deserves world class care.