



Agenda June 29, 2016

- 1. FDA/CPIC interactions (follow-up from last SAB meeting)
- 2. CPIC Table revisions: allele definition table, allele and diplotype frequency tables, diplotype “translation” implementation table
- 3. CPIC guideline implementers/resource page
- 4. CPIC calls: attendance, presentations from implementers
- 5. Engaging 3rd party payers
- 6. Term standardization manuscript in press
- 7. Requests to translate guidelines into foreign languages

FDA/CPIC

- Michael A. Pacanowski, Pharm.D., M.P.H.
Associate Director for Genomics and Targeted Therapy
Office of Clinical Pharmacology, Office of Translational
Sciences
Center for Drug Evaluation and Research
- E. David Litwack
 - Personalized Medicine Staff
 - OIR/CDRH/FDA
 - Review of variant databases

CPIC guideline tables

- Allele function assignment with citations
- Implementation tables
 - Possible diplotypes
 - Interpretation notes
 - Pre- and post-test alerts
- Allele definition table
- Frequency tables
 - Allele frequency by “race” group
 - Diplotype frequency by “race”
 - Phenotype frequency by “race”
 - References
 - Change log

CPIC resources page: implementers



[Guidelines](#) [Genes-Drugs](#) [Alleles](#) [Publications](#) [Resources](#) [Informatics](#) [Members](#) [Contact](#)

Implementation

The following is a list of PGx implementers who are using CPIC guidelines as part of a program to facilitate use of genetic tests to guide prescribing for patients in clinical care settings:

| Institution | Website and/or Contact (if available) |
|--|---|
| BJC Healthcare | |
| Children's Hospital Minnesota | |
| Cincinnati Children's Hospital Medical Center | CCHMC Genetic Pharmacology Service |
| Clearview Cancer Institute | Emily K Pauli; emily.pauli@ccihsv.com |
| Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology | Matthias Schwab; matthias.schwab@ikp-stuttgart.de |
| Erasmus MC | Ron van Schaik; r.vanschaik@erasmusmc.nl |
| Geisinger Health System | Geisinger Health System Genomic Medicine Institute |
| Icahn School of Medicine at Mount Sinai | Stuart Scott lab Aniwaa Owusu Obeng; aniwaa.owusu-obeng@mssm.edu |
| I.M.P. Institute of Predictive Medicine | I.M.P. Institute of Predictive Medicine , info@impredictiva.es |

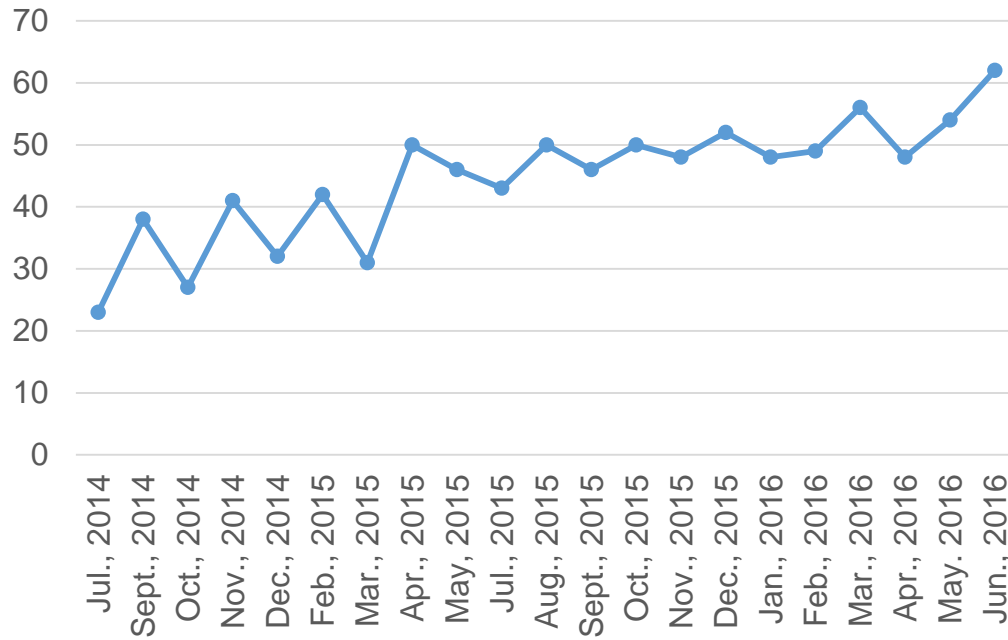
| | |
|---|---|
| UPMC Presbyterian University Hospital | |
| University of South Florida College of Pharmacy | Teresa Vo; teresavo@health.usf.edu |
| Vanderbilt University | My Drug Genome Program Julie Field; Julie.field@Vanderbilt.edu |
| Washington University in St. Louis | |

The following is a list of commercial laboratories and companies who are using CPIC guidelines to aid in the interpretation of genetic tests results (self-reported):

| Company | NIH's Genetic Testing Registry Link or company contact (if applicable) |
|------------------------|--|
| Aegjs | http://www.ncbi.nlm.nih.gov/gtr/labs/505511/ |
| Genelex | http://www.ncbi.nlm.nih.gov/gtr/labs/500170/ |
| Translational Software | Houda Hachad; houda.hachad@translationalsoftware.com |

If you would like your institution to be listed on this page, please send an email to cpic@pharmgkb.org requesting to be listed and provide one or both of the following: institution and website OR contact name and email. (Note: If you are a commercial genetic testing laboratory, you must first submit your information to the Genetic Testing Registry at <http://www.ncbi.nlm.nih.gov/gtr/docs/submit/> and supply the GTR URL to be listed on the implementers site. Other companies may submit a contact email. Send email to cpic@pharmgkb.org with the GTR URL.)

CPIC Monthly Call Attendance



CPIC Conference Call Implementation Presentations

- Cleveland Clinic
- Northshore Hospital, Chicago
- Mt. Sinai
- Center for Addiction and Mental Health, Toronto
- University of Florida Health
- St. Jude Children's Research Hospital
- Vanderbilt University Medical Center

Engaging 3rd party payers

STANDARDIZING TERMS FOR CLINICAL PHARMACOGENETIC TEST RESULTS: CONSENSUS TERMS FROM THE CLINICAL PHARMACOGENETICS IMPLEMENTATION CONSORTIUM (CPIC)

- Authors: Kelly E. Caudle, Pharm.D., Ph.D.1, Henry M. Dunnenberger, Pharm.D.2, Robert R. Freimuth, Ph.D. 3, Josh F. Peterson, M.D. 4, Jonathan D. Burlison, Ph.D.1, Michelle Whirl-Carrillo, Ph.D. 5, Stuart A. Scott, Ph.D. 6, Heidi L. Rehm, Ph.D. 7, Marc S. Williams, M.D. 8, Teri E. Klein, Ph.D. 5, Mary V. Relling, Pharm.D.1, James M. Hoffman, Pharm.D. M.S.1
- Genetics in Medicine July 2016

Final Terms-Allele function

| Term/Gene Category | Final Term* | Functional Definition | Example diplotypes/alleles |
|------------------------------------|--------------------|--|----------------------------|
| Allele Functional Status-all genes | Increased Function | Function greater than normal function | <i>CYP2C19*17</i> |
| | Normal Function | Fully functional/wild-type | <i>CYP2C19*1</i> |
| | Decreased Function | Function less than normal function | <i>CYP2C19*9</i> |
| | No Function | Non-functional | <i>CYP2C19*2</i> |
| | Unknown Function | No literature describing function or the allele is novel | <i>CYP2C19*29</i> |
| | Uncertain Function | Literature supporting function is conflicting or weak | <i>CYP2C19*12</i> |

Final Terms-Phenotype

| Term/Gene Category | Final Term* | Functional Definition | Example diplotypes/alleles | Term/Gene Category |
|---|--------------------------|---|---|---|
| Phenotype-Drug Metabolizing Enzymes (CYP2C19, CYP2D6, CYP3A5, CYP2C9, TPMT, DPYD, UGT1A1) | Ultra-rapid Metabolizer | Increased enzyme activity compared to rapid metabolizers. | Two increased function alleles, or more than 2 normal function alleles | <i>CYP2C19*17/*17</i> <i>CYP2D6*1/*1XN</i> |
| | Rapid Metabolizer | Increased enzyme activity compared to normal metabolizers but less than ultra-rapid metabolizers. | Combinations of normal function and increased function alleles | <i>CYP2C19*1/*17</i> |
| | Normal Metabolizer | Fully functional enzyme activity | Combinations of normal function and decreased function alleles | <i>CYP2C19*1/*1</i> |
| | Intermediate Metabolizer | Decreased enzyme activity (activity between normal and poor metabolizer) | Combinations of normal function, decreased function, and/or no function alleles | <i>CYP2C19*1/*2</i> |
| | Poor Metabolizer | Little to no enzyme activity | Combination of no function alleles and/or decreased function alleles | <i>CYP2C19*2/*2</i> |
| Phenotype-Transporters (SLCO1B1) | Increased Function | Increased transporter function compared to normal function. | One or more increased function alleles | <i>SLCO1B1*1/*14</i> |
| | Normal Function | Fully functional transporter function | Combinations of normal function and/or decreased function alleles | <i>SLCO1B1*1/*1</i> |
| | Decreased Function | Decreased transporter function (function between normal and poor function) | Combinations of normal function, decreased function, and/or no function alleles | <i>SLCO1B1*1/*5</i> |
| | Poor Function | Little to no transporter function | Combination of no function alleles and/or decreased function alleles | <i>SLCO1B1*5/*5</i> |
| Phenotype-High risk genotype status (HLA-B) | Positive | Detection of high-risk allele | Homozygous or heterozygous for high-risk allele | <i>HLA-B*15:02</i> |
| | Negative | High risk-allele not detected | No copies of high-risk allele | |

Next Steps

- Endorsed by Association of Molecular Pathology
- Used in IOM's DiGITIZE Action Collaborative implementation guides
- LOINC-Terms accepted December 2015
- Using in CPIC guidelines

CPIC guidelines in Foreign Languages

Pharmacogenes for ACMG list

- TPMT

Acknowledgements

- PGRN
- PharmGKB
 - Teri Klein
 - Russ Altman
 - Michelle Whirl-Carrillo
 - PharmGKB curators
- CPIC members/observers
- CPIC informatics working group
 - James Hoffman
 - Michelle Whirl-Carrillo
 - Bob Freimuth
- CPIC Steering Committee
 - Mary Relling
 - Julie Johnson
 - Teri Klein
 - Dan Roden
 - Rachel Tyndale



CPIC issues to discuss

- How best to assess usage of CPIC guidelines?
- How to improve interactions with external groups?
- How to prioritize given limited resources?
- Plan for sustainability over time
- How to interact with SAB?
- Timeline: grant renewal application likely due summer of 2017

Guidelines.gov

| Number of CPIC guideline page views reported by guidelines.gov (through July 2015) | | |
|---|-------------|------------|
| Title | Date Posted | Page Views |
| Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and abacavir dosing. | 7/26/2013 | 10159 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for human leukocyte antigen-B genotype and allopurinol dosing. | 7/26/2013 | 10253 |
| Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. | 7/26/2013 | 14623 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. | 7/26/2013 | 10171 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. | 2/14/2014 | 7648 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing. | 2/14/2014 | 6961 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450 2D6 genotype and codeine therapy: 2014 update. | 8/29/2014 | 12543 |
| Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing. | 8/29/2014 | 1842 |
| Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for IFNL3 (IL28B) genotype and PEG interferon-α-based regimens. | 8/29/2014 | 2054 |
| Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for ivacaftor therapy in the context of CFTR genotype. | 12/5/2014 | 1738 |
| The Clinical Pharmacogenetics Implementation Consortium guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update. | 3/13/2015 | 11874 |
| Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for rasburicase therapy in the context of G6PD deficiency genotype. | 3/13/2015 | 1223 |



New Results

Relative Citation Ratio (RCR): A new metric that uses citation rates to measure influence at the article level

Bruce Ian Hutchins, Xin Yuan, James M Anderson, George M Santangelo

doi: <http://dx.doi.org/10.1101/029629>

Abstract

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Metrics

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Posted October 22, 2015.

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Cancer Biology

Cell Biology

Developmental Biology

Ecology

Evolutionary Biology

Genetics

Genomics

Immunology

Abstract

Despite their recognized limitations, bibliometric assessments of scientific productivity have been widely adopted. We describe here an improved method that makes novel use of the co-citation network of each article to field-normalize the number of citations it has received. The resulting Relative Citation Ratio is article-level and field-independent, and provides an alternative to the invalid practice of using Journal Impact Factors to identify influential papers. To illustrate one application of our method, we analyzed 88,835 articles published between 2003 and 2010, and found that the National Institutes of Health awardees who authored those papers occupy relatively stable positions of influence across all disciplines. We demonstrate that the values generated by this method strongly correlate with the opinions of subject matter experts in biomedical research, and suggest that the same approach should be generally applicable to articles published in all areas of science. A beta version of iCite, our web tool for calculating Relative Citation Ratios of articles listed in PubMed, is available at <https://icite.od.nih.gov>.

iCite is a tool to access a dashboard of bibliometrics for papers associated with a portfolio. Users upload the PubMed IDs of articles of interest (from SPIRES or PubMed), optionally grouping them for comparison. *iCite* then displays the number of articles, articles per year, citations per year, and Relative Citation Ratio (a field-normalized metric that shows the citation impact of one or more articles relative to the average NIH-funded paper). A range of years can be selected, as well as article type (all, or only research articles), and individual articles can be toggled on and off. Users can download a report table with the article-level detail for later use or further visualization.

[Launch *iCite*](#)

cites/year of each paper, normalized to the citations per year received by NIH-funded papers in the same field and year. A paper with an RCR of 1.0 has received the same number of cites/year as the average NIH-funded paper in its field, while a paper with an RCR of 2.0 has received twice as many cites/year as the average NIH-funded paper in its field. (Average high-impact Nature article ~ 4).

| Year | Title | Authors | RCR |
|------|--|---|-------|
| 2013 | Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing. | Caudle, K E; Thorn, C F; Klein, T E; Swen, J J; McLeod, H L; Diasio, R B; Schwab, M | 4.44 |
| 2013 | Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. | Scott, S A; Sangkuhl, K; Stein, C M; Hulot, J-S; Mega, J L; Roden, D M; Klein, T E; Sabatine, M S; Johnson, J A; Shuldiner, A R; | 8.97 |
| 2013 | Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing. | Leckband, S G; Kelsoe, J R; Dunnenberger, H M; George, A L; Tran, E; Berger, R; Müller, D J; Whirl-Carrillo, M; Caudle, K E; Pirmohamed, M; | 4.92 |
| 2013 | Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. | Hicks, J K; Swen, J J; Thorn, C F; Sangkuhl, K; Kharasch, E D; Ellingrod, V L; Skaar, T C; Müller, D J; Gaedigk, A; Stingl, J C; | 10.66 |
| 2013 | Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing: 2013 update. | Relling, M V; Gardner, E E; Sandborn, W J; Schmiegelow, K; Pui, C-H; Yee, S W; Stein, C M; Carrillo, M; Evans, W E; Hicks, J K; Schwab, M; Klein, T E | 9.59 |
| 2013 | Clinical Pharmacogenetics Implementation Consortium guidelines for human leukocyte antigen-B genotype and allopurinol dosing. | Hershfield, M S; Callaghan, J T; Tassaneeyakul, W; Mushiroda, T; Thorn, C F; Klein, T E; Lee, M T M | 6.19 |
| 2012 | The clinical pharmacogenomics implementation consortium: CPIC guideline for SLCO1B1 and simvastatin-induced myopathy. | Wilke, R A; Ramsey, L B; Johnson, S G; Maxwell, W D; McLeod, H L; Voora, D; Krauss, R M; Roden, D M; Feng, Q; Cooper-Dehoff, R M; Gong, L; Klein, T E; Wadelius, M; Niemi, M; | 7.69 |
| 2012 | Clinical pharmacogenetics implementation consortium guidelines for HLA-B genotype and abacavir dosing. | Martin, M A; Klein, T E; Dong, B J; Pirmohamed, M; Haas, D W; Kroetz, D L; | 4.52 |
| 2012 | Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P450 2D6 (CYP2D6) genotype. | Crews, K R; Gaedigk, A; Dunnenberger, H M; Klein, T E; Shen, D D; Callaghan, J T; Kharasch, E D; Skaar, T C; | 13.47 |
| 2011 | Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. | Johnson, J A; Gong, L; Whirl-Carrillo, M; Gage, B F; Scott, S A; Stein, C M; Anderson, J L; Kimmel, S E; Lee, M T M; Pirmohamed, M; Wadelius, M; Klein, T E; Altman, R B; | 9.68 |
| 2011 | Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450-2C19 (CYP2C19) genotype and clopidogrel therapy. | Scott, S A; Sangkuhl, K; Gardner, E E; Stein, C M; Hulot, J-S; Johnson, J A; Roden, D M; Klein, T E; Shuldiner, A R; | 8.86 |
| 2011 | Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. | Relling, M V; Gardner, E E; Sandborn, W J; Schmiegelow, K; Pui, C-H; Yee, S W; Stein, C M; Carrillo, M; Evans, W E; Klein, T E; | 11.04 |
| | CPIC: Clinical Pharmacogenetics Implementation | | 9.61 |



CPIC meetings

- **CPIC luncheon meeting**—open to CPIC members
 - Thursday March 10th, 2016 Noon-1:30 PM
 - Hilton Bayfront Hotel, San Diego, CA
 - Email: kelly.caudle@stjude.org to attend

- **CPIC Meeting** (a specialty meeting of the PGRN)
 - Wednesday March 15th, 2017
 - Marriott Wardman Park Hotel, Washington DC
 - Further details pending.

CPIC Term Standardization for Clinical Pharmacogenetic Test Results Project

CPIC (Clinical Pharmacogenetics Implementation Consortium) is leading an effort to standardize terms for clinical pharmacogenetic tests. The goal of the project is to create standardized terms to be used in CPIC guidelines (specifically Tables 1 and 2) and in the larger pharmacogenetics community. A list of phenotype term options based on an extensive literature review and scanning of sample laboratory reports is being developed. Refinement of the terms will be performed using a modified Delphi method in the context of expert opinions.

- Read more CPIC's proposal for [Term Standardization for Clinical Pharmacogenetic Test Results: alleles and phenotypes](#) .
- The first round of the Delphi process has been completed. See the [Delphi 1 survey results by question](#) .

- To standardize phenotype terms in the CPIC guidelines and harmonize terms with external groups (e.g., ClinGen, IOM, etc.) to facilitate use in Electronic Health Records
 - Allele functional status terms (Table 1 in guideline)
 - Low, absent, high, intermediate
 - Phenotype (i.e. from diplotypes; Table 2 in guideline)
 - UM, EM, IM, PM

CPIC website: www.cpicpgx.org

CPIC guidelines and list of CPIC genes/drugs



CPIC announcements

CPIC information

Upcoming meetings: CPIC members on 3/10/2016 and open meeting on 3/15/2017

What is CPIC?

The Clinical Pharmacogenetics Implementation Consortium (CPIC) was formed as a shared project between PharmGKB and the Pharmacogenomics Research Network (PGRN). CPIC guidelines are peer-reviewed and published in a leading journal (in partnership with *Clinical Pharmacology and Therapeutics*) with simultaneous posting to PharmGKB with supplemental information/data and updates. Anyone with clinical interests in pharmacogenetics is eligible for membership. CPIC's goal is to address some of the barriers to implementation of pharmacogenetic tests into clinical practice.

Background

One barrier to clinical implementation of pharmacogenetics is the lack of freely available, peer-reviewed, updatable, and detailed gene/drug clinical practice guidelines. CPIC provides guidelines that enable the translation of genetic laboratory test results into actionable prescribing decisions for specific drugs. The guidelines can center on genes (e.g. thiopurine methyltransferase and its implications for thiopurines) or around drugs (e.g. warfarin and CYP2C9 and VKORC1). Priority is given to genotyping tests that are already offered in CLIA-approved clinical settings.

Team

Leader

News & Announcements

[DIGITizE Suggests Implementing 2 CPIC Guidelines in CDS](#)

Posted by Michelle Whiri-Carrillo on 12/17/2015

The DIGITizE Action Collaborative has suggested that Clinical Decision Support (CDS) be implemented based on CPIC's ... [read more](#)

[CPIC Upcoming Meetings – Save the Date!](#)

Posted by Michelle Whiri-Carrillo on 12/9/2015

The Clinical Pharmacogenetics Implementation Consortium is holding a meeting for members in 2016 and an open meeting in ... [read more](#)

[Framework Published to Guide Development of PGx Public Policy, Applied in Canada](#)

Posted by Allison Fohner on 12/7/2015

The paper, "The 3-I framework: a framework for developing public policies regarding pharmacogenomics (PGx) testing in Canada" ... [read more](#)

[Article on PGx by Dean Julie A. Johnson in The Conversation](#)

Posted by Julia Barbarino on 11/21/2015


Dean Julie A. Johnson, Dean of the College of Pharmacy, Distinguished Professor of Pharmacy

Coming soon: List of implementers

CPIC slides

Overview Presentation

This presentation describes CPIC, the underlying assumptions of CPIC guidelines, the guideline development process and how the guidelines can be implemented in a clinical setting.

 [Overview Presentation \(.pptx\)](#)


CPIC projects

Term Standardization for Clinical Pharmacogenetic Test Results

CPIC is leading an effort to standardize terms for clinical pharmacogenetic tests. The goal of the project is to create standardized terms to be used in CPIC guidelines (specifically Tables 1 and 2) and in the larger pharmacogenetics community. A list of phenotype term options based on an extensive literature review and scanning of sample laboratory reports is being developed. Refinement of the terms will be performed using a modified Delphi method in the context of expert opinions.

 [Brief overview](#) of the project and final results (.pptx)


 [Proposal](#) for Term Standardization for Clinical Pharmacogenetic Test Results: alleles and phenotypes (.pdf)

 [Delphi 1](#) survey results by question (.pdf)

 [Delphi 2](#) survey results (.pdf)

 [Delphi 3](#) survey results (.pdf)

 [Delphi 4](#) survey results (.pdf)

 [Final terms](#) for the CPIC Term Standardization Project (.pdf)

CPIC logo

CPIC Logo Graphics

Logo image files that you can use for referring to CPIC. The images are in PNG and SVG format.

| | | | | |
|---|---|---------------------------------|---------------------------------|---------------------|
| logo without full name | 200px width PNG | 400px width PNG | 600px width PNG | SVG |
| logo with full name | 200px width PNG | 400px width PNG | 600px width PNG | SVG |
| logo source (& other logos) | Adobe Illustrator (.ai) | | | |

CPIC Dosing Guideline for [simvastatin](#) and [SLCO1B1](#)

last updated 06/30/2014

Summary

The FDA recommends against 80mg daily simvastatin dosage. In patients with the C allele at SLCO1B1 [rs4149056](#), there are modest increases in myopathy risk even at lower simvastatin doses (40mg daily); if optimal efficacy is not achieved with a lower dose, alternate agents should be considered.




Find genotype-based dosing recommendation

Pick rs4149056 alleles:

Annotation

June 2014 Update

Advance online publication 9 July 2014.

- The [2014 update of CPIC guideline regarding SLCO1B1 and simvastatin-induced myopathy](#), has been published in Clinical Pharmacology and Therapeutics. CPIC extensively reviewed the literature from February 2011 to December 2013 and concluded the dosing recommendations provided in the 2012 CPIC guideline for SLCO1B1 and simvastatin-induced myopathy have not changed. However, this updated guideline also provides a brief review regarding SLCO1B1 genotype and risk of myopathy for other statins. Furthermore, comprehensive translation tables mapping SLCO1B1 genotypes to coded genotype/phenotype summaries, EHR priority result notation and interpretation (consultation) text were created to facilitate incorporation of SLCO1B1 pharmacogenetics into an electronic health record with clinical decision support.*
- This guideline is applicable to:
 - adult patients
 - pediatric patients
- Excerpt from the 2014 simvastatin dosing guideline:
 - "For simvastatin, the evidence linking myopathy to [rs4149056](#) in SLCO1B1 is of high quality, and this association has been reproduced in randomized trials and clinical practice-based cohorts. Conversely, the association of [rs4149056](#) with myopathy has been less compelling for other statins. We therefore focus this guideline on simvastatin."
 - "In 2011 and updated in 2013, the FDA added warnings to the simvastatin product label to direct providers away from initiating at the 80 mg simvastatin dose."
 - "At lower simvastatin doses (e.g., 40 mg daily), it is our position that SLCO1B1 genotype (if available) could be used to warn providers about modest increases in myopathy risk for patients with a C allele at [rs4149056](#). In these circumstances, we recommend a lower dose of simvastatin or use an alternative statin (e.g. pravastatin or rosuvastatin) and we also highlight the potential utility of routine CK surveillance (Table 2). If patients with a C allele at [rs4149056](#) do not achieve optimal LDL cholesterol-lowering efficacy with a lower dose (e.g. 20 mg) of simvastatin, we recommend the prescribing physician consider an alternate statin based on (i) potency differences (i.e., use a lower dose of a higher potency statin such as atorvastatin, rosuvastatin, or pitavastatin), (ii) drug-drug interactions (e.g., boceprevir, clarithromycin, cyclosporine, strong CYP3A4 inhibitors, etc.), and (iii) relevant co-morbidities (e.g., trauma, significant renal impairment, post-solid organ transplant, thyroid disease etc.)."
 - "At the time of this writing, there are no data available regarding SLCO1B1 genotype effects on simvastatin response or myopathy in pediatric patient populations, although there is no reason to suspect that the polymorphisms in SLCO1B1 will affect simvastatin's metabolism differently in children compared to adults."
- Download and read:
 - [The Clinical Pharmacogenetics Implementation Consortium \(CPIC\) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update](#) 
 - [2014 supplement](#) 
 - [2014 SLCO1B1 translation table](#) 

CPIC guidelines are
posted on PharmGKB
(www.pharmgkb.org)



CPIC guidelines linked to “Practice Guideline” filter on PubMed

NCBI Resources How To

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Article types

✓ Practice Guideline

Review

More ...

Text availability

Abstract available

Free full text available

Full text available

Publication

dates

5 years

10 years

Custom range...

Species

Humans

Other Animals

Clear all

Show additional filters

Display Settings: ☑

Results: 15

Filters activated: Practice Guideline. [Clear all](#) to show 12158 items.

1. [Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing.](#)

Caulde KE, Thorn CF, Klein TE, Swen JJ, McLeod HL, Diasio RB, Schwab M.
Clin Pharmacol Ther. 2013 Dec;94(6):640-5. doi: 10.1038/clpt.2013.172. Epub 2013 Aug 29.
PMID: 23988873 [PubMed - indexed for MEDLINE] [Free PMC Article](#)
[Related citations](#)

2. [Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update.](#)

Scott SA, Sangkuhl K, Stein CM, Hulot JS, Mega JL, Roden DM, Klein TE, Sabatine MS, Johnson JA, Shuldiner AR; Clinical Pharmacogenetics Implementation Consortium.
Clin Pharmacol Ther. 2013 Sep;94(3):317-23. doi: 10.1038/clpt.2013.105. Epub 2013 May 22.
PMID: 23698643 [PubMed - indexed for MEDLINE] [Free PMC Article](#)
[Related citations](#)

3. [Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing.](#)

Leckband SG, Kelson JR, Dunnenberger HM, George AL Jr, Tran E, Berger R, Müller DJ, Whirl-Carrillo M, Caulde KE, Pirmohamed M; Clinical Pharmacogenetics Implementation Consortium.
Clin Pharmacol Ther. 2013 Sep;94(3):324-8. doi: 10.1038/clpt.2013.103. Epub 2013 May 21.
PMID: 23695185 [PubMed - indexed for MEDLINE] [Free PMC Article](#)
[Related citations](#)

4. [Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants.](#)

Hicks JK, Swen JJ, Thorn CF, Sangkuhl K, Kharasch ED, Ellingrod VL, Skaar TC, Müller DJ, Gaedigk A, Stingl JC; Clinical Pharmacogenetics Implementation Consortium.
Clin Pharmacol Ther. 2013 May;93(5):402-8. doi: 10.1038/clpt.2013.2. Epub 2013 Jan 16. Review.
PMID: 23486447 [PubMed - indexed for MEDLINE] [Free PMC Article](#)
[Related citations](#)

5. [Clinical Pharmacogenetics Implementation Consortium guidelines for human leukocyte antigen-B genotype and allopurinol dosing.](#)

Hershfield MS, Callaghan JT, Tassaneeyakul W, Mushiroda T, Thorn CF, Klein TE, Lee MT.

New feature

Try the new Display Settings option - Sort by Relevance

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[pharmacogenetics pharmacogenomics](#)

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[Proton pump inhibitors in pediatrics : mechanism of action, pharmacokinetic \[Paediatr Drugs. 2013\]](#)

[Pharmacogenetics and personalized treatment of type 2 diabetes. \[Biochem Med \(Zagreb\). 2013\]](#)

[Pharmacogenetics and cardiovascular disease-implications for personaliz\[Pharmacol Rev. 2013\]](#)

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[Review Role and implications of nanodiagnosics in the cf \[Saudi J Biol Sci. 2014\]](#)

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Clin Pharmacol Ther. 2013 Dec;94(6):640-5. doi: 10.1038/clpt.2013.172. Epub 2013 Aug 29.

Clinical Pharmacogenetics Implementation Consortium guidelines for dihydropyrimidine dehydrogenase genotype and fluoropyrimidine dosing.

Caudle KE¹, Thorn CF, Klein TE, Swen JJ, McLeod HL, Diasio RB, Schwab M.

Author information

Abstract

The fluoropyrimidines are the mainstay chemotherapeutic agents for the treatment of many types of cancers. Detoxifying metabolism of fluoropyrimidines requires dihydropyrimidine dehydrogenase (DPD, encoded by the DPYD gene), and reduced or absent activity of this enzyme can result in severe, and sometimes fatal, toxicity. We summarize evidence from the published literature supporting this association and provide dosing recommendations for fluoropyrimidines based on DPYD genotype (updates at <http://www.pharmgkb.org>).

PMID: 23988873 [PubMed - indexed for MEDLINE] PMID: PMC3831181 [Free PMC Article](#)

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CPIC is cited in NIH's Genetic Test Registry (GTR) for clinical pharmacogenetic tests

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Thiopurine methyltransferase deficiency

SNOMED CT: Thiopurine methyltransferase deficiency, ID: 238012003

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C R O G Thiopurine methyltransferase deficiency

Associated Genes

[TPMT](#)

Summary: thiopurine S-methyltransferase

Clinical Features

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- Caused by mutation in the thiopurine S-methyltransferase gene (TPMT, 187680.0001)
- Decreased activity of thiopurine S-methyltransferase
- Decreased metabolism of thiopurine drugs
- Hematopoietic toxicity develops on standard doses of thiopurine drugs
- Heterozygotes may also show increased susceptibility to toxic effects of thiopurine treatment

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