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Authoring and Peer Review

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Medical Genetics Summaries (MGS) for pharmacogenetics is a freely-available collection of articles describing how genetics plays a role in an individual's response to drugs or predisposition to disease. Each summary is structured to facilitate quick and easy access to information, including genetic testing and therapeutic recommendations. Medical Genetics Summaries are based on authoritative sources, driven by guidelines, actionable, and undergo an extensive review process as described below.

Editorial Oversight

The MGS editors advise on subject matter, guide the project through developments in the field, provide final approval before publication, and assist in recruiting reviewers and resolution of key issues during the review process.

Selection of Topics

The selection of topics for new MGS chapters is influenced by drugs approved by the U.S. Food and Drug Administration (FDA) that have pharmacogenomic biomarkers in the label, the availability of clinical testing for drug response, the needs of the community, and input from the editors.

To identify new drugs not yet covered in MGS, the author consults the FDA's "Table of Pharmacogenomic Biomarkers in Drug Labeling". To prioritize the order of new MGS chapters, the author checks the Genetic Testing Registry (GTR) for drug response records containing information on genetic testing but lacking summary information on the drug response. The author takes into consideration the current needs of the community, for example adding summaries that support National Institutes of Health (NIH) initiatives like the All of Us research program, Medicine and Your DNA report, and the NIH Helping to End Addiction Long-term (HEAL) Initiative.

Upon the release of a new MGS chapter to the production site, an excerpt is displayed in the relevant GTR and MedGen drug response records. Reciprocal links between MGS, GTR, MedGen, and other National Center for Biotechnology Information (NCBI) resources are also added for better integration and accessibility.

Structured Format

Each MGS drug response chapter follows a structured format with one drug section and one or more gene sections, depending on how many genetic factors have been identified to influence drug metabolism and action.

1. The introductory paragraphs detail the drug, its clinical uses, and how genetic variants influence an individual's response to the drug. Dosing recommendations from the FDA drug labels and practice guidelines from authoritative professional and medical societies are also presented.

2. The drug section begins with a description of the drug, including drug class, mechanism of action, indications for use, and common side effects. This is followed by a discussion on the factors that influence the drug response.
3. The gene section reviews important facts on the gene's role in drug metabolism or action and the nature of variants and how they impact the individual's response to the drug. It also discusses common or clinically significant variants, including their prevalence across different ethnic populations.
4. The "Genetic Testing" section is a key part of the summary, describing available genetic testing options and linking to genetic test providers listed in the NIH GTR. The GTR includes descriptions of clinical and research tests along with phenotype, test targets, and methodologies.
5. The Gene-drug interactions section provides a list of interactions between the gene(s) of note and other medications, including those used in other indications separate from the current chapter. Additional resources to learn more about other medications that may be impacted by variations in the same gene are also included.
6. The "Therapeutic Recommendations based on Genotype" excerpts clinically actionable information, such as dosing recommendations from the FDA drug label, and therapeutic recommendations from pharmacogenetic societies (for example, the Clinical Pharmacogenetics Implementation Consortium [CPIC], the Canadian Pharmacogenomics Network for Drug Safety [CPNDS], The Dutch Pharmacogenetics Working Group [DPWG]) and medical societies (for example, the American Society of Clinical Oncology [ASCO], the American College of Medical Genetics [ACMG], the National Comprehensive Cancer Network [NCCN]). The MGS does not create guidelines or recommendations.
7. The nomenclature table provides information on different terms used for genetic variants. Commonly used terms and historic terms are linked to the official Human Genome Variation Society (HGVS) terms and rs identifiers when available. The table also includes links to relevant resources like ClinVar, dbSNP, and the Pharmacogene Variation (PharmVar) Consortium.
8. Expert reviewers are a vital part of MGS and are acknowledged in every chapter. Information on previous versions of the summary is displayed.

Writing Process

Each summary is authored by our in-house senior medical writer, who holds a PhD with professional experience in pharmacogenomics. All phases, from authoring to production, are tracked in an internal ticket management system.

To create the first draft of a summary:

1. The author consults the most recent FDA drug label for the drug. Additionally, to gain a better understanding of the drug's context of use and the impact of genetic factors, the author uses NIH resources and other clinical sites, such as UpToDate.
2. Next, the author identifies key guidelines and primary research papers, using PubMed Clinical Queries, PubMed, CPIC, and The Pharmacogenomics Knowledgebase (PharmGKB).
3. Finally, the author searches PubMed for the most recent publications. Firstly, to find content that has not yet been cited by guidelines; and secondly, to identify external reviewers who are actively involved in relevant research.

Internal Review

Each summary undergoes internal review involving one or 2 NCBI staff members with experience in genetic counseling or molecular genetics. Once the author has finalized the first draft of a summary, it is submitted for internal review, along with key supporting guidelines (for example, FDA drug label, key guidelines). The internal reviewers perform the first round of expert review, utilizing track changes to ask questions, provide suggestions

and make corrections. This process is documented in a ticket management system, including all versions of the document and comments from the author and reviewers.

External Review

Following the internal review, each summary goes through a scientific peer-review process involving between 2–9 experts from outside NCBI. Typically, the external review includes at least one clinical specialist experienced in prescribing the drug and with published papers on its use, along with one laboratory professional experienced in pharmacogenomics. The comments from expert reviewers are retained in our internal records. After the summary is released to production, all current and previously published versions are stored in the document management system, allowing public access.

Finalizing the Summary

Once all the review comments are reconciled, the summary undergoes in-house copyediting before public release.

Updates

Summaries are scheduled to be updated every 4–6 years or whenever there is an update to guidelines from which excerpts have been taken for the summary. The internal reviewers determine whether updates are minor or major. For minor updates, the summary undergoes internal review and copyediting. Once published, a link to the previous version of the summary is made available. For major updates, the summary is sent out for external review.

Archive

Summaries will be archived if the FDA withdraws approval for the drug. Archived summaries display notices to alert the user that the summary is archived and the information may be out of date, serving as a historical reference only. The notices include the statement: NOTE: ARCHIVED ON [date] BECAUSE [drug name] IS NO LONGER LICENSED FOR USE IN THE USA. THIS SUMMARY IS FOR HISTORIAL REFERENCE ONLY AND WILL NOT BE UPDATED.

Summaries are not deleted, and they remain publicly available for display.

Version history

Each summary displays the created date and the date of its last update. Once a version of the summary is published and made publicly available, the date of publication is logged and displayed.

Access to all versions of the document is provided via links in the Version history section.

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