Clinical Therapeutics provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoeconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition, Clinical Therapeutics features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

Published articles range from pivotal studies exploring new chemical entities in large, multicenter trials to those exploring repurposing of marketed agents. Additionally, pilot studies; reports that assess drug safety and tolerability in all phases of development; new routes of administration and new formulations; pharmacokinetic, bio-availability, and biosimilarity; and changes in practice guidelines and standards, are all of interest for publication. Clinical Therapeutics also understands the importance of strengthening the body of evidence surrounding particular agents through the publication of replication studies, negative trials, and failed trials.

Beyond the clinic, we seek reports that examine the real-world implications of therapeutics such as comparative effectiveness and pharmacoeconomics studies as well as work that has implications for health policy. Commentaries, which include perspectives and contemporary issues, are sought to offer a balance of viewpoints and scholarly opinion on a broad array of drug-related topics. Case reports, which remain a vital part of our mission, offer clinically valuable lessons. All manuscripts are peer reviewed by independent clinicians or scientists for clinical relevance, technical accuracy, methodological rigor, clarity, and objectivity using a blind review process.

In addition to feature articles published monthly, each issue of Clinical Therapeutics features a specific theme section dedicated to an annual update of a specific topic area. A special guest editor will comprise each update with reviews, commentaries, and original research highlighting what's new or controversial in the topical specialty. Authors are invited to submit manuscripts for consideration in the topic updates, identifying submissions as such in their cover letters. Submissions not selected for the updates will be considered for general publication. Submit your manuscript at https://www.editorialmanager.com/clinther.
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Introduction

Clinical Therapeutics provides peer-reviewed, rapid publication of recent developments in drug and other therapies as well as in diagnostics, pharmacoeconomics, health policy, treatment outcomes, and innovations in drug and biologics research. In addition Clinical Therapeutics features updates on specific topics collated by expert Topic Editors. Clinical Therapeutics is read by a large international audience of scientists and clinicians in a variety of research, academic, and clinical practice settings. Articles are indexed by all major biomedical abstracting databases.

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Clinical Therapeutics charges page fees to publish. Page fees are not optional unless the author is approved for a fee waiver (see waiver information below). Please note, page fees as described, are completely separate from the payment option to publish your paper as an Open Access article.

Corresponding authors of manuscripts accepted for publication will be charged the following rates:

- For Original Research papers: A fee of USD $600 per printed journal page is charged for accepted papers; for example, a 10 page paper will be invoiced at $6000
- For Review articles: A flat fee of USD $2500
- For Commentaries, Brief Reports, Pilot Studies, and Case Reports: A flat fee of USD $2000
- For Research Letters: A flat fee of USD $1000
Upon article acceptance and delivery of a composed article proof, payment instructions will be provided to corresponding author with a link to a payment portal ("Submission Start"). Author is expected to complete payment with 48 hours, and to do so, prior to returning article proofs. Please note: author's article will not be published until such time payment has been satisfied.

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ARTICLE TYPES

Original Research

Submissions categorized as Original Research describe substantive, well-controlled clinical research projects including clinical trials, pharmacokinetic/pharmacodynamic studies, meta-analyses, observational studies, health economic evaluations, and epidemiologic studies. Manuscripts should be prepared as described (See PREPARATION AND FORMATTING) and must provide enough detail about the study design, population, interventions, data collection and analysis methods, and outcomes to permit study replication. Data must be original and presented in accordance with journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (eg, CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for meta-analyses).

Abstract: ≤400 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: ≤6000 words, structured as follows: Introduction, Participants and Methods, Results, Discussion, Conclusions
Tables/Figures: ≤8
References: Required, unlimited
Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Reviews
Comprehensive, evidence-based narrative and systematic reviews are welcome. Systematic reviews without meta-analyses are considered and published as Reviews, while systematic reviews with meta-analyses should be submitted as Original Research. For the Pharmacoeconomics, Outcomes, and Health Policy section, only systematic reviews will be considered. Authors should contact the editorial office to discuss the topic area to avoid duplication with previously submitted or accepted manuscripts.

Systematic reviews should critically assess available data on a specific topic relevant to clinical practice, disease prevention, diagnostics, therapeutics, or health policy. Systematic reviews should follow PRISMA guidelines (http://www.prismastatement.org/index.htm) and include a PRISMA-style flow diagram (as a Figure or Supplemental Material) and checklist for review. The Methods section should identify the databases that were searched, search terms used, and inclusion/exclusion criteria for identified articles; an assessment of the validity of reviewed studies; and a summary that includes future directions for studies in this area. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. While not required, prospective registration of systematic review protocols is strongly encouraged. If available, the protocol registration number, registry name, and URL should be indicated in the Methods. Systematic reviews should be identified as such in the title or subtitle.

Abstract: ≤400 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: ≤6000 words, structured as follows: Introduction, Methods, Results. Discussion, Conclusions
Tables/Figures: ≤6
References: Required, unlimited
Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Narrative reviews should provide up-to-date information relevant to clinical practice, public health, or clinical-stage development of therapeutics and/or diagnostics. Narrative reviews should not focus solely on the authors’ own work. Narrative reviews should include an Introduction that describes the background, purpose, and perspective of the article; a Methods section that describes the approach and literature search criteria (if any). A separate Results section is not required. Each study mentioned in the review should include the study design, a description of the study population (age range, disease/severity), the dose and duration of each treatment administered, and the data and P values to accompany any valid comparisons. Discussion of pre-clinical data is permitted to complement discussion of therapeutic/diagnostic strategies and their development. Narrative reviews must be identified as such in the Abstract and Methods.

Abstract: ≤400 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: ≤6000 words, structured as follows: Introduction, Methods, Results (optional), Discussion, Conclusions
Tables/Figures: ≤6
References: Required, unlimited
Supplemental Material: Allowed, unlimited length (See Supplemental Material)

Commentaries
These papers should address an important and current issue in clinical practice, health policy, or therapeutics/diagnostics research from the author’s perspective. All clinical recommendations should be supported by relevant published guidelines or peer-reviewed literature. Evidence-based statements must be clearly distinguished from author opinion. Discussion of pre-clinical data is permitted to complement discussion of therapeutic/diagnostic strategies and their development. The submission should include a descriptive title, a brief Abstract, an Introduction, pertinent information detailing the position of the paper, a Discussion, a Conclusion (which may be part of the discussion), and references.

Abstract: ≤300 words, unstructured (See Abstract)
Keywords: 4-6 terms
Main Text: 3000-3500 words, structured as follows: Introduction, Discussion, Conclusions
Tables/Figures: ≤5
References: ≤60, required
Supplemental Material: Not permitted

**Brief Reports**
These papers are reports of preliminary clinical investigations that are narrowly focused or provide limited findings. The submission should include a descriptive and succinct title, a structured Abstract, an Introduction that specifies the importance of the study, a Methods section, Results, a Discussion, a Conclusion, and references. Although these submissions are shorter in length, Brief Reports must adhere to the journal's ethical requirements and data reporting policies (See EDITORIAL POLICIES).

Abstract: ≤250 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: 2000-3000 words, structured as follows: Introduction, Methods, Discussion, Conclusions
Tables/Figures: ≤3
References: ≤30, required
Supplemental Material: Allowed, unlimited (See Supplemental Material)

**Pilot Studies**
A pilot study is a preliminary, exploratory, preparatory, small-sample effort undertaken to decide whether a larger study is warranted. The sample size is too small to permit generalizability, but it should provide a window into what a larger trial would look like. The submission should include a descriptive and succinct title, a structured Abstract, an Introduction that specifies the importance of the study, a Methods section, Results, a Discussion, a Conclusion, and references. Pilot Studies must adhere to the journal's ethical requirements and data reporting policies (See EDITORIAL POLICIES).

Abstract: ≤250 words, structured (See Abstract)
Keywords: 4-6 terms
Main Text: 2000-3000 words, structured as follows: Introduction, Methods, Discussion, Conclusions
Tables/Figures: ≤3
References: ≤30, required
Supplemental Material: Allowed, unlimited (See Supplemental Material)

**Research Letters**
These letters are focused on previously published studies from which new findings have been generated. Since methods and other informative material are contained in the original paper, they can be referenced rather than repeated. Alternatively, research letters can describe novel or hypothesis-generating research that may stimulate further investigation or alert readers to clinically relevant but preliminary findings. These submissions should include a descriptive and succinct title; an Introduction that specifies the rationale for the report, beginning with a statement similar to "This communication provides..."; a description of any new methods and results; a Discussion/Conclusion section; and selected references. Please note that Research Letters may be chosen, at the editor's discretion, to be published online only. In such instances, authors will be informed of this decision at acceptance and are free to withdraw their submission. Online only articles are indexed and are available in full text or PDF formats identical to that of print articles.

Abstract: None
Keywords: None
Main Text: 1000-2000 words, structured as follows: Introduction, Methods, Discussion, Conclusions
Tables/Figures: ≤2
References: ≤30, required
Supplemental Material: Not permitted

**Case Reports**
Case reports are retrospective analyses of one, two, or three clinical cases. Case reports are an important part of post-marketing surveillance. They serve an alerting function by informing about new, unusual, or unexpected events. These events may be adverse drug reactions, drug-drug interactions, or drug-disease interactions. Before submitting a case report, the author(s) must conduct a thorough literature search as well as a review of product labeling when a drug is involved. This will reduce the reporting of what may already be well known.
Reports of suspected adverse drug reactions should provide a description of the event, details regarding the implicated medication (e.g., purpose, when initiated), effects of discontinuation or re-challenge, treatment for the reaction, and duration of patient follow-up, if any. Evidence for causality must be strong. In the case of adverse drug events, use of the Naranjo Adverse Drug Reaction probability scale to determine the likelihood that the events were drug-related (Naranjo CA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-245) is recommended. The manufacturer of the drug in question should be notified regarding any event before publication.

Importantly, authors should clearly indicate in the cover letter whether the case was part of a larger study or meta-analysis, and whether the case was reported in aggregate elsewhere.

The report should include a descriptive, succinct title; an introduction; a well-documented case description; discussion; conclusions; and references. The Introduction should announce the subject and purpose of the report, including statements of why the case is important and how the literature search was performed. The Case Description should include a narrative account of the case with brief, pertinent clinical, laboratory, and medication information. The Discussion should comment on evidence that the case is new or unusual and consider possible alternative explanations for case features. The Conclusions should provide a summary of the adverse drug reaction-medication relationship, how to treat it, and how to avoid it. (For more information about what constitutes a good case report, see Vandenbroucke JP. In defense of case reports and case series. Ann Intern Med. 2001;134:330-334 and DeBakey L, DeBakey S. The case report. I. Guidelines for preparation. Int J Cardiol. 1983;4:357-364.)

To be considered, authors must provide documentation of patient informed consent to publish, which can be attached to the cover letter. All identifying information must be masked per HIPAA guidelines prior to submission. (See Ethical Considerations for Case Reports).

Please note that Case Reports may be selected, at the editor's discretion, to be published online only. Additionally, authors may be asked to reduce the length of the report substantially if similar cases were reported previously. In such cases, authors will be informed of the decision to forgo print at acceptance. Online only articles will be indexed and available as full text or PDF, identical to that of print articles.

Abstract: None
Keywords: 4-6
Main Text: 1500-3500 words, structured as follows: Introduction, Case Description, Discussion, Conclusions
Tables/Figures: ≤2
References: ≤15, required
Supplemental Material: Not permitted

Letters to the Editor
These are objective, constructive, or educational critiques of papers published in Clinical Therapeutics. Accepted letters will be sent to the author of the original paper for a response. Each letter and response is published together. Alternatively, letters may focus on topical issues that are of interest to readers of

Abstract: None
Keywords: None
Main Text: ≤1000 words, unstructured
Tables/Figures: ≤1
References: Required, ≤5
Supplemental Material: Not permitted

Video Articles
Clinical Therapeutics encourages authors who have presented a talk at a meeting to convert their talk into a video production for online publication. Interested authors are encouraged to view the following example: Untangling tau imaging. Alzheimers Dement (Amst). 2016;4:39-42. A pre-submission inquiry is required for this type of submission. See Video Article Guidelines for preparation instructions.

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The basic elements of all submissions are as follows, and details on each item are provided below. Manuscripts, tables, figures, and supplemental material must be submitted in their original file formats; do not submit PDFs.1 Document Requirement Cover Letter Required ICMJE Form(s) Required for each author Declaration of Interest Required Title Page Required Highlights Required for Original Research Graphical Abstract Optional Manuscript File (without author details) Required for new and revised submissions Tables Optional Figures Optional Supplemental Material Optional for Original Research, Reviews, Brief Reports, and Pilot Studies Response to Review Rquired for revised submissions Marked Manuscript File (with tracked changes, without author details) Required for revised submissions

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**Blinded manuscript (no author details):** The main body of the paper (including the legends, references, and any acknowledgments) should not include any identifying information, such as the authors' names or affiliations.

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- Name of the Special Section in which the paper is to be included, if applicable
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• **Author declaration of individual contribution.** All authors must have materially participated in the research and/or article preparation, so individual roles for all authors must be described. (See Author Contributions). Add this information here if not using the CRediT roles.

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Highlights are mandatory for Original Research as they help increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any). Please have a look at the examples here: example Highlights.

Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

**Graphical Abstract**

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

Authors can make use of Elsevier's Illustration Services to ensure the best presentation of their images and in accordance with all technical requirements.

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The manuscript file should contain the following items: title, abstract, clinical trial registration (if applicable), keywords, main text, acknowledgments, figure/table legends, references. These items are described in detail below. All author names and identifying information must be removed from the manuscript file to facilitate double-blind peer review. The manuscript file should be structured according to article type, be double-spaced, include page numbers, and follow AMA style except as indicated below (See Style).

**Title**

The title should be concise, informative, and focused on the study objective. Statements about the conclusion(s) of the work should be avoided. Randomized controlled trials, meta-analyses, and systematic reviews should be identified as such in the title. Subtitles can be used to provide supplementary information (e.g., study design); however, titles should be able to stand alone. Use nonproprietary drug names (See Names of Drugs and Devices); avoid abbreviations and formulae where possible.
Abstract

Abstracts should be structured or unstructured according to article type and word limits as detailed below. Abstracts are often presented separately from the article; therefore, must be able to stand alone. References should be avoided (if essential, the complete reference per AMA style must be given within the lines of text). Non-standard or uncommon abbreviations should be avoided (when necessary, they must be defined at their first use in the abstract).

Structured abstracts are required for Original Research (≤400 words), Reviews (≤400 words), Brief Reports (≤250 words), and Pilot Studies (≤250 words). Structured abstracts should contain sufficient detail as directed by the extension to the CONSORT statement for abstracts, and should be formatted as follows:

Purpose: Briefly provides the frame of reference for the reader and identifies the knowledge gap that the article seeks to address; clearly states the purpose of the research; and identifies the scientific hypotheses and questions being asked.

Methods: Succinctly describes study methodology, including study design, study dates, setting/data sources, inclusion and exclusion criteria, interventions, outcomes, statistical approaches, and adverse event assessment methodology.

Findings: Provides demographics of the study population, including sex, age range, and numbers of participants in each group; reports principle data and outcomes in a quantitative fashion, including effect sizes and confidence intervals or $P$ values; includes adverse events.

Implications: Covers any limitations or problems in interpretation or generalization from the study findings as well as implication and future directions; must be strictly limited to what can be supported directly by the Findings, and what was identified in the Purpose section.

For manuscripts that require clinical trial registration (See Reporting and Registration of Clinical Trials), the name of the trial registry, trial registration number, and URL of the registry should be included immediately following the Implications section of the abstract.

Unstructured abstracts are required for Commentaries (?300 words). Unstructured abstracts should briefly describe the importance and clinical relevance of the topic, the objective, approach, and a summary of key points. Abstracts are not required for Research Letters, Case Reports, and Letters to the Editor.

Keywords

Immediately after the abstract, provide 4-6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, ‘and’, ‘of’). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

Body of Manuscript

The main text should adhere to word limits and structure according to article type as detailed above. All submissions should adhere to journal policies (See EDITORIAL POLICIES) and EQUATOR Reporting Guidelines for the applicable study design (eg, CONSORT for randomized trials, STROBE for observational studies, CHEERS for economic evaluations, PRISMA for systematic reviews and meta-analyses).

Introduction: State the objectives/hypotheses of the work and provide an adequate background; avoid a detailed literature survey or a summary of the results. Required for all article types except Letters to the Editor.

Methods: Provide sufficient detail to allow the work to be replicated by others. Methods already published should be indicated by a reference: only relevant modifications should be described. For work involving human subjects, describe the (1) study design and randomization procedures; (2) study dates and setting; (3) institutional review board (RB) approval or waiver, including name of the IRB/ethics committee; (4) details of patient consent or assent of youth and children; (5) participants and conditions/factors studied, including full inclusion and exclusion criteria; (6) interventions, if any, with full description of placebo, sham, or control conditions [See Placebos in Clinical Trials]; (7) primary and secondary outcome measures, including whether secondary analyses were pre-specified; (8) detailed statistical analyses, with a priori significance thresholds, methods for handling missing data or outliers if applicable, and any relevant citations. Rationale for inclusion of only one sex or age group should be provided and scientifically justified [See Inclusion of Sex and Gender]. Systematic
reviews and meta-analyses should follow PRISMA guidelines. Subheadings (up to two additional levels) are encouraged. A Participants and Methods section is required for Original Research, Brief Reports, Pilot Studies, and Research Letters. A Methods section is required for Reviews.

Results: The Results should be clear, concise, and relevant to the stated objectives/hypotheses. Describe the study population first, including sex, age, and other relevant demographic characteristics of subjects. All numeric data should be reported with descriptive and/or inferential statistical test results (including exact p-values, if available). For each outcome, report results for each group, the effect size, and its precision (ie, 95% confidence interval). Do not discuss implications or limitations in this section. Tables, figures, and subheadings (up to two additional levels) are encouraged. Results are required for Original Research (including meta-analyses), systematic Reviews, Brief Reports, and Pilot Studies; optional for narrative Reviews.

Discussion: The Discussion should explore the importance and relevance of the results of the work, not repeat them. Authors should critically examine the work, describe unexpected and/or contradictory findings, and address any limitations of the study design or statistically indeterminate results here. All inferences must be supported by evidence presented in the Results section. Authors should also discuss generalizability and clinical implications of findings, as well as any future studies needed. Avoid extensive citations and discussion of published literature. Subheadings (up to one additional level) are permitted. A Discussion is required for all article types except Letters to the Editor; a combined Results and Discussion section is often appropriate for narrative Reviews.

Conclusions: The main conclusions of the study should be present.

Acknowledgments
Collate acknowledgments in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided materials or assistance during the research (eg, language help, writing assistance, or proofreading the article, etc). Do NOT list the names of authors or funder(s) in this paragraph.

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Pre- or post-marketing studies must undergo review by an institutional review board (IRB) or ethics committee. Patients must give written informed consent unless a waiver of consent is allowed by the IRB. Patients must be informed of any real or potential conflicts of interest, including compensation of the investigator and potential costs to the patient that may result from their participation in the study. The amount of the remuneration of the investigators for their participation in pre- or post-marketing studies must be approved by the IRB/ethics committee. If the design of a prospective pre- or post-marketing study calls for a treatment intervention such as a switch or withdrawal, then criteria must be established a priori for patient selection, the implementation of the intervention, and assessment of success/failure of such intervention. Such criteria must be scientifically justified, documented, uniformly applied and enforced, and clearly reported in the study report. Additionally, the patient or his/her insurance provider will not be required to pay for costs related to prospective interventions, such as those that may result from a drug switch or withdrawal.

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This journal has adopted the proposal from the International Committee of Medical Journal Editors (ICMJE) which require, as a condition of consideration for publication of clinical trials, registration in a public trials registry such as https://clinicaltrials.gov, which can be used by all countries. In addition to a listing in https://www.clinicaltrials.gov, submitting authors should also include the identification number received from trials listed in http://www.controlled-trials.com, another registry recognized by the World Health Organization and the International Committee of Medical Journal Editors. The controlled-trials site provides listings to trials at various stages -- complete, in process, proposed. Please note that requirements for registration may change so authors should always check that they
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A full description of any placebo (PBO) or matched control used in a clinical trial must be given in the Methods section. It will no longer be sufficient to simply indicate that a PBO was used. This means that color; type (capsule or pill or liquid); contents (eg, lactose) including dyes; taste (if there is any); and packaging (eg, double-dummy) must be noted. For solid PBOs, shape must also be described, as well as whether the PBO is active or inactive. In addition, any efforts to study the success of matching should be included. For example, could subjects/patients or evaluating/rating clinicians guess assignments? Sham procedures must also be described in detail. We are instituting this change as part of our ongoing effort to facilitate replication of findings from trials. All too often this valuable information is omitted from published trial results. When appropriate these descriptions may be designated as Supplemental Digital Content. For more information, see Shader RI. Placebos, Active Placebos, and Clinical Trials. Clin Ther. 2017;39(3):451-454.

**Safety and Tolerability**
For submissions to *Clinical Therapeutics*, a statement about safety should explicitly include the time period and only when there is a clear absence of harm as determined by relevant questioning, observation, and testing. It is possible that a drug or biologic may be considered tolerable at the same time that tests show it to be unsafe (e.g., a lengthened QTc interval). Conversely, a drug may be considered safe by all objective assessments, and yet produce side effects that can contribute to high degrees of dose interruption or discontinuation. Furthermore, a drug may also be considered prima facie unsafe when pharmacogenomic information suggests it will yield unwanted metabolites in certain individuals or be highly prone to clinically significant drug interactions with frequently used additional agents or foods. Safety assessments may need to be different for different age groups (e.g., effects on growth and development in children and youth, increased propensity to falls in the elderly, effects on life style for active adults). It is also important to remember that safety concerns may stem from excipients added during the manufacturing process rather than from the drug or biologic per se.) For more information, see Shader RI. Safety Versus Tolerability. Clin Ther. 2018;40(5):672-673.

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