



302 knights run ave. • suite 800 • tampa, fl 33602 • 813.258.4747 • 813.259.1585 fax • goldstandard.com

Submission Request

Date: February 11, 2008

Full Identification of Compendium: *Clinical Pharmacology*

Publisher: Gold Standard Inc., Elsevier Health Sciences

Edition: Continual updating of subscription-based, electronic online publication at:

<http://www.clinicalpharmacology.com>.

NOTE: The *Clinical Pharmacology* compendium is also available for intranet release, updated monthly. A CD product distributed quarterly is available to selected customers.

Contact Information:

MaryAnne Hochadel PharmD, BCPS

Vice President, Editor-in-Chief

Gold Standard Inc./ELSEVIER

hochadel.m@goldstandard.com

813-579-3871

AND

Kathleen J. Vieson, PharmD, BCOP

Vice President, Director of Clinical References

Clinical Pharmacology Product Manager

Gold Standard Inc./ELSEVIER

vieson.k@goldstandard.com

813-579-3905

Address:

ELSEVIER/Gold Standard Inc.

302 Knight's Run Ave

Suite 800

Harbor Island

Tampa FL 33602

Action Requested:

Gold Standard Inc. and Elsevier strongly urge the Centers for Medicare and Medicaid Services (CMS) to officially recognize *Clinical Pharmacology* as a new addition to the mandated reference list for Medicare coverage decisions regarding the appropriate use of drugs and biologics for patients with cancer, as specified in Section 1861(t)(2)(B)(ii)(I) of the Social Security Act. Gold Standard Inc. and Elsevier request this consideration via the CMS-established process described in the Federal Register Notice Volume 72, Number 133, July 12, 2007.

About Gold Standard Inc.:

Based in Tampa, Florida, Gold Standard Inc. is a leading developer of drug information databases, software and clinical information solutions. The Company's products are developed by a staff of highly trained professionals with extensive experience in pharmacy practice, electronic publishing and software development. Gold Standard's parent company, Elsevier (www.elsevier.com), is a world-leading publisher of scientific, technical and medical information products and services with more than 7,000 employees in over 70 offices across 24 countries.

About the Clinical Pharmacology Compendium:

Clinical Pharmacology, compared to other established drug compendia, is relatively new to the landscape, and was first launched in 1994. The compendium has grown and evolved in scope and is now utilized nationwide in many retail pharmacy chains, pharmacy benefits management organizations, managed care environments, and long-term care providers. We additionally serve several oncology-focused clients, including US Oncology and over 1000 community and academic health care institutional settings within the United States. Drug monographs from the *Clinical Pharmacology* editorial team are also available to physicians and allied health care professionals thru Elsevier products such as MD Consult, Nursing Consult, and OncologyStat. *Clinical Pharmacology* also provides the drug information data within eMPowerX, a complete, secure, wireless patient care and e-prescribing solution from Gold Standard Inc. used in state-provided programs such as Florida, Mississippi, and Louisiana Medicaid. Finally, *Clinical Pharmacology* is an accepted professional drug compendium by ALL 50 State Boards of Pharmacy.

Clinical Pharmacology's focus is to provide unbiased, comprehensive, accurate, relevant, and timely drug information to health care professionals. A peer-review process drives the inclusion of information within the database. The compendium is formatted and electronically driven in database format to allow fast point-of-care referencing and information solutions, such as drug-drug interaction alerting, in direct patient care environments.

Clinical Pharmacology employs doctoral-level pharmacists, many with Board Certification by the Board of Pharmaceutical Specialties, to proactively monitor the medical literature and U.S. drug regulatory activity in accordance with Gold Standard Editorial Policy. Board Certified Oncology Pharmacotherapy Specialists (BCOP) are employed to edit the Oncology focused content. These individuals have specific knowledge of Oncology regimens and are active licensed practitioners. A complete listing of the editorial team and contributors is available at: http://www.clinicalpharmacology.com/marketing/editorial_team.html

Two independent, published research studies reported *Clinical Pharmacology* as a superior electronic reference as compared to several other tertiary online drug compendia, with the highest overall composite scores for clinical dependability and completeness. The questions, which covered a wide range of issues including availability, compatibility, drug dosage and indications, mechanism of action, drug identification, drug interactions, storage and stability, herbal products and dietary supplements, and newly approved and investigational drugs, were based on largely on inquiries received and identified as clinically important by the Butler University Drug Information Center and the Nova Southeastern University Drug Information Department, respectively.

References:

Peak AS, Girt A, Butler University College of Pharmacy and Health Sciences. Comparison of Tertiary Drug Information Databases. Presented at: American College of Clinical Pharmacy (ACCP) Annual Meeting, October 23-26, 2005. San Francisco California. Abstract 75. *Pharmacotherapy* 2005; 25 (Number 10): 1449.

Clauson, K, Seamon M, Marsh W, et al., Nova Southeastern University College of Pharmacy. Evaluation of the Functionality of Subscription and Free Online Drug Information Databases. 11th World Congress on Internet in Medicine. October 14-19, 2006. Ontario Canada. Abstract. MedNet Congress 2006, page 34. Available at: <http://yi.com/mednet06/draft-mednet2006book.pdf>

The following describes, in concise fashion, how the Clinical Pharmacology Compendium fulfills the definition and desired characteristics of a drug compendium as defined by the MedCAC.

1. Extensive Breadth of Listings:

Clinical Pharmacology meets CMS's definition of a compendium.

Clinical Pharmacology provides information regarding greater than 50,000 medication products, inclusive of U.S. FDA-approved prescription medicines, non-prescription (OTC) medicines, many dietary supplements, and investigational drug agents. The database includes a comprehensive listing of the drugs and biologics used in the treatment and management of patients with cancer within the United States. Clinical data are presented in greater than 2600 clinical drug monographs, and drug and biologic products are indexed to these monographs.

The data in *Clinical Pharmacology* monographs include:

- Generic (ingredient) name
- Brand names of marketed products, NDCs and other official marketed product information, inclusive of dosage forms, strengths, package sizes
- Applicable Anatomic, Pharmacologic, and Therapeutic classes
- Monographs incorporate all concepts from official FDA-approved product labeling
- Administration directions (off-label administration data clearly denoted)
- FDA-approved and other studied Indications and Dosages for specific diseases, including dosage for special populations or dosage adjustments (off-label uses clearly denoted)
- Pharmacology discussions
- Pharmacokinetics
- Contraindications
- Warnings/precautions, including Boxed Warnings
- Interactions and related reports (drug/drug, drug/food, drug/supplement) and suggestions for managing them, in both healthcare professional and consumer language
- Adverse effects
- Monitoring test/parameter highlights
- Greater than 2200 Consumer Medication Information (MedCounselor) Handouts

Notes: FDA is Food and Drug Administration; NDC is National Drug Code

Compendium Special Features:

A sophisticated search function within *Clinical Pharmacology* allows practitioners to quickly navigate, access, compare, and reference drug information by generic and brand names, anatomic, pharmacologic and therapeutic classifications, indications, contraindications, drug interactions, adverse reactions, and patient education (MedCounselor) sheets. Data within the monographs also include explicit pharmacology, pharmacokinetics, and administration data. Information is available for multiple populations, including Adults, Elderly, Adolescents, Children, Infants, and Neonates as applicable. Off-label indications are clearly distinguished from labeled indications via the use of a “dagger” indicator on the indication or administration data within the monograph content and from indications index searches. To better inform health care professionals in a decision-making, an advanced search capability allows practitioners to choose multiple qualifiers to compare medications or refine medication lists based on precautions or other known patient characteristics, such as renal impairment or hepatic disease. A drug comparison report is available that helps practitioners compare drugs by indications and other indicators side by side in informative charts.

2. Quick Processing from Application for Inclusion to Listing:

Clinical Pharmacology is fed by a proprietary database for editorial workflow that allows for real-time editing at any time of day from any global location. The database system ensures the peer-review process and allows specific content benchmarking. The electronic archives allow us to quickly identify content dating and specific, historical editorial changes to content.

An average of 500-600 clinically-based updates to drug monographs per month are included in the *Clinical Pharmacology* database (range, 350 to 2000 per month). Such clinical updates include changes in regulatory product labeling or FDA approvals, MedWatch alerts, and the citing of new medical literature. In one year's time, greater than 60% of the entire compendium is refreshed with such changes.

An average regulatory or literature update, including a new drug approval, takes between 1-4 weeks to be edited and peer-reviewed after identification of the relevant literature search or regulatory action.

If the update is of great urgency, such as when a medication is formally recalled from FDA approval or the U.S. market, or a significant safety issue has been identified, the editorial system and processes of peer-review allow the initial flow of the critical information to our online subscribed customers within hours of the released media or literature information.

3. Detailed description of the evidence reviewed for every individual listing:

Individual indications for a drug are clearly noted as FDA-approved or off-label (dagger indicator). Off-label uses incorporate and actively reference the relevant and current literature citations. Not all studies reviewed by the editors may be referenced for the compendium, as the intent is to provide the health care practitioner with the most useful, relevant, and clinically-sound data available to support the use of the drug for the listed indication in humans. These references are usually sound, high level, randomized, controlled clinical trials incorporating phase III data and may also include associated expert clinical practice guidelines which incorporate medically-accepted evidence for appropriate treatment and care of patients with the condition/indication. Lesser quality evidence may be acceptable for rare or refractory diseases; however, if cited they are qualified by disclosure of the reference quality within the listing. Phase I study data are intentionally not incorporated. A concise, yet sufficiently detailed description summarizing the referenced literature and its quality are presented within the text of the off-label listing.

A summary of the editorial policy for *Clinical Pharmacology*, including the editorial peer-review process is available at: http://www.clinicalpharmacology.com/marketing/editorial_policy.html

The Gold Standard Inc. Off-Label Data for Drug Information Products policy, is available at: http://www.clinicalpharmacology.com/marketing/off_label.html

4. Use of prespecified published criteria for weighing evidence AND

5. A prescribed published process for making recommendations:

The Gold Standard Inc. Editorial Team adheres to a specific editorial policy for the creation of all drug information content, and the process is peer-reviewed. The policy defines the content creation and peer-review process used for drug information and indications listings. A description of the literature retrieval process, including the incorporation of appropriate evidence, is included.

Determining credible inputs to content is critical to the quality of our drug information data. Acceptable references are approved by the Editor-in-Chief and are reiterated through content development policy. The editorial team establishes a hierarchy of data credibility with preference given to those publications embracing a peer-reviewed publication methodology. Gold Standard maintains internal data files for content updates and these include relevant data used in content development.

Off-label data for indications and dosage are included in our drug information content when identified as a clinically-relevant or emerging treatment by the Editorial Staff. Off-label data are primarily identified and selected by the Editorial Staff for inclusion in the database through regular and comprehensive review of:

- Primary published literature
- New or updated national practice guidelines
- Surveillance of other accepted sources of medical information (e.g., FDA, CDC, NIH communications)
- Dialogue with customers or other external reviewers of our content, particularly practitioners within the specialty field

Off-label information may be included in the monographs of FDA-approved drugs, investigational drugs, or dietary supplements.

The members of the Editorial Staff conduct a thorough search of the primary literature and other accepted sources of information to identify relevant, published information, including negative or equivocal findings. Searches ensure that relevant and timely publications are considered.

After the research is completed, the evidence is reviewed and independently evaluated by the assigned Editorial Staff member. If the documentation is deemed sufficient to warrant inclusion, the data undergo peer-review for inclusion into our content. The documentation for the off-label data includes supporting references of the best-quality evidence available from our research, and will often include a summary of the level of quality of the supporting evidence in descriptive fashion. All off-label (i.e., non-FDA-approved) indications, dosage, or related data are clearly designated within the content of our products.

In the evaluation of the research available, the following are considered:

- The impact (benefits and risks) of the therapy on the disease/condition (e.g., emerging treatment, response vs. conventional therapy, optional use when there is approved therapy failure, etc.)
- Patient safety

Patient safety is an especially important consideration. Despite sufficient literature evidence that may justify an off-label practice, the lack of FDA-approval for that use means that the drug is not given the same degree of scientific scrutiny as for an approved indication. Scientific evidence documenting the efficacy of off-label use in routine practice settings often does not replicate the depth and breadth of the evidence the manufacturer is required to provide the FDA to receive drug approval for a specific indication. In addition, the population studied or the off-label indication may be so different from the approved indication that extrapolating safety data from the approved documents can be an erroneous presumption.

Please note that the Editorial Staff adheres to the Consumer Medication Information (CMI) Guidance of the FDA with regard to the production of Patient Information Documents (i.e., MedCounselor Sheets). With rare exceptions, the MedCounselor Sheets refrain from noting specific off-label uses to consumers.

A summary of the editorial policy for Clinical Pharmacology, including the editorial peer-review process is available at: http://www.clinicalpharmacology.com/marketing/editorial_policy.html

The Gold Standard Inc. Off-Label Data for Drug Information Products policy, is available at: http://www.clinicalpharmacology.com/marketing/off_label.html

6. Publicly transparent process for evaluating therapies:

As noted, summaries of our processes are readily viewable to the public. We also welcome further inquiries and make available our staff for discussion of the processes and sources used in creating content.

7. Explicit “Not recommended” listing when validated evidence is appropriate:

As defined in the Gold Standard Inc. Off-Label Data for Drug Information Products policy: Unsupported or inconclusive data within Clinical Pharmacology are qualified within the text of the monograph, and are referenced. For example, unsupported or refuted indications are often mentioned only in the Description section of the drug monograph for completion and will not usually be found in the Indications or Dosage sections. This prevents unsupported or not-recommended uses from being actively indexed in our interactive reports regarding appropriate indications for a drug’s use. In essence, if a use is not clinically-appropriate, a mention will be made of the inappropriate use, but it will not be included within the clinically actionable content of the indications and dosage of the monograph.

8. Explicit listing and recommendations regarding therapies, including sequential use or combination in relation to other therapies:

Clinical Pharmacology does not report the use of drug agents as sole entities in treatment, but reports the data, when applicable, in the context of sequential or regimen-based use within the indications and dosage section of the drug monograph. This is especially prevalent within the drug compendium content relevant to the Oncology arena, where the sequential use of a drug or biologic or its use in the context of a regimen is often the norm.

9. Explicit “equivocal” listing when validated evidence is equivocal:

As defined in our Editorial policy, inconclusive data within *Clinical Pharmacology* are definitively qualified within the text, and are referenced. This is particularly important in today’s environment where non-inferiority trials have become relatively widespread within the medical literature.

10. Process for public identification and notification of potential conflicts of interest of the compendia’s parent and sibling organizations, reviewers, and committee members, with an established procedure to manage recognized conflicts:

Gold Standard Inc. maintains a conflict of interest policy that is readily transparent to the public. A summary of the editorial conflict of interest policy for Clinical Pharmacology is available for public review at:

http://www.clinicalpharmacology.com/marketing/editorial_policy.html

Editorial team authors, reviewers, and board members annually disclose to Gold Standard Inc. any potential conflicts of interest on a standardized corporate form. The disclosures are placed on file with the organization. If conflicts are identified, then the organization has a defined process by which to manage the conflict in a way that promotes unbiased content production. The specific policy for our editorial team employees is as follows: Pharmaceutical Industry/Conflict of Interest Relationship Policy

Gold Standard is committed to providing unbiased, complete, and accurate drug information. It is important to define the Editorial Team policy regarding relationships with manufacturers of drug products. The Editorial Content Development Process Summary outlines the editorial peer-review process for our database content. Individual editorial team members may have past relationships with the industry, as the knowledge and skills obtained from such a position are beneficial to the mission of the Gold Standard team: provision of complete, timely, and accurate drug information. Current direct relationships with any pharmaceutical company or their representative are not acceptable. Editors may not be employees or receive payment for rendered services from such companies.

Sponsored programs, events, publications, or the like can be presented/written by editors as long as the content is not dictated, suggested, or reviewed by the sponsoring company; the program must be supported by an unrestricted grant from the pharmaceutical industry corporation sponsoring the service. Editors may receive benefits from the pharmaceutical industry extended to any participant attending a professional conference or continuing education session. Gold Standard editorial team members cannot accept individualized gifts or benefits.

Further information regarding this policy, including past employment relationships, is on file at Gold Standard. Any financial information contained in the file is confidential. For any questions regarding policy documentation, please contact us at 1-800-375-0943, 813-258-4747 or email info@goldstandard.com.

In Summary:

The *Clinical Pharmacology* Compendium is widely recognized by health care professionals and corporations nationwide and globally as a reliable, credible, authoritative, accurate, timely, and comprehensive drug information source. The Editorial Team produces the content via an independent, predefined, and peer-reviewed process to ensure the appropriateness of the presented clinical data.

Gold Standard Inc. recognizes that evidence-based clinical drug information, and the technology by which such information is driven, are in a constant state of evolution. Such evolution is vital to the industry. We recognize that all compendia may have unique attributes that allow them to meet the desired characteristics of a CMS-recognized publication and the individualized needs of the health care professionals and patients served by the various compendia.

Gold Standard Inc. appreciates the opportunity to be considered and requests that CMS add *Clinical Pharmacology* to the list of authoritative compendia specified in Section 1861(t)(2)(B)(ii)(I) of the Social Security Act.

If you have any questions related to this request, please contact MaryAnne Hochadel as indicated in the contact listing.

Respectfully Submitted,



MaryAnne Hochadel, Pharm.D., BCPS
Vice President, Editor-in-Chief

ELSEVIER / Gold Standard
302 Knight's Run Avenue, Suite 800 Tampa, FL 33602
+1 813-579-3871 | office