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JEREMIAH W. (JAY) NIXON, GOVERNOR • BRIAN KINKADE, INTERIM DIRECTOR

MO HEALTHNET DIVISION

P.O. BOX 6500 • JEFFERSON CITY, MO 65102-6500

WWW.DSS.MO.GOV • 573-751-3425

Dear Interested Party:

The MO HealthNet Pharmacy Program prior authorizes all new drug entities, and new drug product dosage forms of existing drug entities. New drug entities are defined as products that have been approved by the Food and Drug Administration (FDA), and are available on the market. These products are identified from First Data Bank (FDB) weekly pricing update reports, as being unique within a FDB classified Generic Code Number (GCN). The prior authorization restrictions will continue through the review process and creation of recommendations which are presented quarterly to the Division's Advisory Groups. New drug prior authorization edit criteria follow the product's FDA approved indications.

The MO HealthNet Division (MHD) clinical staff performs the reviews of the identified new drug products. Once identified, the new drugs are then immediately coded as "Prior Authorization required." For unrestricted drug status consideration for your product, a more detailed review request should be presented to MHD. These product submissions should generally follow the AMCP guideline format. Enclosed are the abbreviated AMCP guidelines which contain the Division's minimum requirements for product information submission. Full AMCP dossiers are welcome.

If you have any questions concerning the new drug submission process, or the policy surrounding the prior authorization of all new drugs, feel free to contact me at Rhonda.Driver@dss.mo.gov or (573) 751-6961.

Sincerely,

Rhonda Driver, R.Ph.
Director of Pharmacy
Pharmacy & Clinical Services

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MO HEALTHNET NEW DRUG GUIDELINES

1. Executive Summary – Clinical and Economic Value of the Product – Justify the value of the product. The manufacturer should articulate a value argument to justify these expected expenditures for this product in the context of its anticipated effects on the clinical evidence, health outcomes, and the economic consequences for the healthcare system.
 - 1.1 Clinical Benefits – FDA approved indication , short synopsis (1-2 paragraph) of the efficacy and safety information (from the prescribing information and clinical trials and summarize (1 page maximum) the clinical benefits of the proposed therapy in terms of : a) Efficacy and Effectiveness, b) Safety/tolerability and c) Shortcomings of current treatment and the unmet medical need that the proposed therapy addresses.
 - 1.2 Economic Benefits Summary (1 page maximum) in terms of: a) Cost per unit, b) Context of the proposed cost (potential clinical benefits provided and potential economic benefits) and c) Shortcomings of other therapies. Also briefly present results of observational research or economic data (PMPM or ICER) and summarize other published information on the cost or economic impact of the product.
 - 1.3 Conclusions (1/2 page maximum) – Summarize the value of the proposed therapy in 1-2 paragraphs highlighting key points regarding the clinical and economic advantages and uniqueness of the product and include a statement regarding the expected impact of the product, relative to other available treatment options both pharmaceutical and non-pharmaceutical.
2. Product Information and Disease Description
 - 2.1 Product Description (20 pages maximum) NOTE: Verbatim language from the package insert should not be supplied here. If there is not substantive data and information that can be provided beyond what is in the PI, these sections should be left blank and the reader referred to the copy of the PI which is in the Appendix.
 - Generic, brand name, and therapeutic class of the product.
 - All dosage forms, including strengths and package sizes.
 - NDC (National Drug Code) for all formulations
 - WAC cost per unit size
 - Federal Rebate percent.
 - Supplemental Rebate percent.
 - AHFS or other Drug Classification
 - FDA approved (or other studied) indications. Include detailed discussion of the approved FDA indications and the date the approval was granted (or expected to be granted). Other significant off-label uses and potential new indications being studied.
 - Pharmacology
 - Pharmacokinetics/Pharmacodynamics
 - Contraindications
 - Warnings/Precautions
 - Adverse Effects
 - Interactions, include:
 - Drug/Drug

- Drug/Food
- Drug/Disease
- Dosing and Administration
- Access, e.g. restrictions on distribution, supply limitations, anticipated shortages, and/or prescribing restrictions.
- Co-Prescribed / Concomitant Therapies, including dosages, and recommended use of other agents or treatments with the product.
- Concise comparison of PI information with the primary comparator products in the same therapeutic area to include: dosing, indications, pharmacokinetic/pharmacologic profile, adverse effects, warnings, contraindications, interactions and other relevant characteristics. Direct head-to-head trials should be noted here and the reader referred to the review of those trials in Section III of the dossier.

2.2 Place of the product in therapy (those with multiple indications the following information should be provided for each indication. Do not duplicate information presented in Sections 3.0, 4.0 and 5.0)

2.2.1 Disease Description (1-2 pages maximum per disease) – The intent is to give the reader a brief but good overall sense of the disease. It should provide a description of specific patient subpopulations in which the drug is expected to be most effective, if known. Include clinical markers, diagnostic or genetic criteria, or other markers, if known, that can be used to identify these subpopulations. Summarize each topic in table or bullet format. Disease description should include epidemiology, relevant risk factors, pathophysiology, clinical presentation and societal, humanistic and/or economic burden.

2.2.2 Approaches to Treatment (1-2 pages maximum per major indication) – The key questions to address are: How is the disease/condition currently treated? How does the new product fit into standard existing therapy? Provide a VERY brief summary of information from the literature for each topic but do not duplicate information included in other sections. Include:

- Approaches to treatment – principal options / practice patterns
- Description of alternative treatment options (both drug and non-drug)
- Place of the proposed therapy in treatment (e.g. first line)
- Proposed ancillary disease or care management intervention strategies
- Expected outcomes of therapy
- Description of other drug development or post-marketing obligations as required by the FDA such as a REMS, Phase IV trial, patient registry, restricted distribution channel and other elements designed to assure the safe use of the product.
- Other key assumptions and their rationale.

2.2.3 Relevant Treatment Guidelines and Consensus Statements from National and/or International Bodies – Description of treatment guideline's position on the therapy.

2.1. Evidence for Pharmacogenomic Tests and Drugs – the following evidence should be presented as appropriate in support of submissions involving pharmacogenomic testing:

- Analytic Validity
- Clinical Validity
- Clinical Utility
- Cost Effectiveness

3. Supporting Clinical Evidence

3.1. Summarizing Key Clinical Studies (2 pages maximum per study) – Summaries of all relevant clinical studies that have been conducted, whether published or not, should be included in each of the categories listed in Sections 3.1.1 and 3.1.2 (all relevant economic studies should be included in Section 5). Avoid duplication, if a study reported both clinical and economic outcomes, include the study summary in this section. Tabulate the clinical results in Section 3.1.1 and in Section 5 refer to the summary description in Section 3.1. Economic outcomes should be tabulated in Section 5. All of the following items that apply should be included in the study summaries:

- Name of the clinical trial or study and publication citation(s)
- Objective, location and study date
- Trial design, randomization and blinding procedures
- Setting, inclusion and exclusion criteria
- Sample characteristics (demographics, number studied, disease severity, comorbidities)
- Drop-out rates and procedures for handling drop-outs (ITT, per protocol, etc.)
- Treatment: dosage regimens, washout period, etc.
- Clinical outcome(s) measures to include outcomes evaluated and delineate primary vs. secondary study endpoints and their corresponding results
- Other outcome measures (e.g., patient-reported outcomes) which should include principal findings
- Statistical significance of outcomes and power calculations
- Validation of outcomes instruments
- Generalizability of the population treated
- Study limitations, as stated by the authors
- Publication citation(s)/references used including finding source of the study

Use the following criteria to determine relevance:

- Relevant studies that provide clinical information that may impact formulary decisions, including but not limited to safety (including total number of patients exposed to the drug, efficacy, effectiveness and comparative effectiveness, and identification of patient subgroups, practice settings, etc., in which use of the drug may be more appropriate.
- All Phase 3 clinical trials
- In general, include all large, randomized controlled trials
- Smaller studies, e.g., Phase 2 trials, only if they contain relevant information that is not provided by larger studies
- Include studies conducted in settings outside the US if they add new information not contained in the U.S. Trials
- Do not include basic pharmacologic studies, e.g., Phase 1 studies
- Do not include purely pharmacokinetic studies, unless the value proposition is based on the pharmacokinetic properties of the product, or the studies identify

an appropriate patient subgroup.

3.1.1 Include all relevant published and Unpublished Clinical Studies supporting labeled indications:

- Placebo-controlled safety and efficacy trials
- Prospective effectiveness and comparative effectiveness trials, including pragmatic trials
- Open-label safety extension studies
- Prospective studies examining other non-economic endpoints such as health status measures and patient-reported outcomes. If the instruments utilized in these studies are supported by previous validation and reliability studies, also reference these studies
- Unpublished data: Provide as much detail as can be disclosed.

3.1.2 Include all Published and Unpublished Data and Clinical Studies supporting Off-Label Indications:

- Include all relevant studies of the types listed in 3.1.1 above
- Include off-label indications that are reasonably likely to be considered by practitioners, based on the available supporting evidence. Provide contact information for the questions about other uses.
- Unpublished data: Provide as much detail as can be disclosed.
- This constitutes an unsolicited request for all relevant studies supporting off-label use of the product.

Additional items:

- Include relevant data and findings from the Center for Drug Evaluation and Research's Office of Drug Safety.
- Include confirmation that trials for the product are registered in a public trials registry and provide access information.
- Include list of ongoing clinical trials and links to their registry information.

3.1.3 Clinical Evidence Spreadsheets of All Published and Unpublished Trials – Evidence tables should include the following data elements:

- Citation (if unpublished, give abstract information or indicate “data on file”)
- Treatments
- Sample size and length of follow-up
- Inclusion/exclusion criteria
- Design
- Primary Endpoints
- Secondary Endpoints
- Results: Provide an explicit statement of effect size, not just relative risk reduction and/or statistical significance. Within the Results column, include a table of key results
- Statistical significance

3.1.4 Summary of Evidence from Secondary Sources – (1 page maximum per source). The following may be submitted. Summaries should be concise, focusing only on the major conclusions:

- Cochrane Collaboration systematic reviews
- Formal, published systematic reviews from peer-reviewed journals

- Agency for Healthcare Research and Quality (AHRQ) evidence summaries
- Health technology assessments from other recognized agencies, public or private, including reviews from other countries
- Evidence-based clinical practice guidelines, medical society position statements, etc. These documents should include explicit evidence grading criteria
- Compendia officially recognized by the Secretary of Health and Human Services that list the drug. If these references are available only by subscription, provide PDF documents or reprints of the relevant content.

4.0 Economic Value and Modeling Report (maximum 20 pages)

4.1 Modeling Overview – present an overview of the rationale, approach, and suggested methods for developing a decision-analytic based cost-effectiveness model with the intent of the model to quantify for the healthcare system the risk-benefit tradeoff of the product, and its economic value.

4.1.1 Utility of Modeling for Decision- Making – Decision-analytic based, cost-effectiveness models are one of the best available means to assess the overall potential value of healthcare technologies. Decision models can provide:

- An explicit framework for decision-making
- Synthesis of evidence on health consequences and costs from many different sources
- Formal assessment of uncertainty
- A quantitative measure of clinical risk-benefit
- Explicit and evaluable assumptions
- Specificity for a product’s role or place in therapy
- Benchmarks against which the product’s future performance can be measured.

4.1.2 Types of Models

- Cost-effectiveness models should be based on healthcare costs and health outcomes, including cost-effectiveness, cost-consequences, and cost-utility analyses. Highly recommended to be included.
- Budget impact models should be based on drug cost, ADE costs, and disease offset costs. Useful when using ISPOR guidelines.
- Financial models should be based on drug cost only. Not recommended because they do not address clinical or economic value.

4.1.3 Modeling Methods

- More than one perspective can be used but payer perspective should be included.
- Timeframe can be variable
- Discounting should be applied at 3% for costs and effects, but undiscounted results for clinical events and life expectancy are also useful
- Briefly note strengths/weaknesses of model types

4.1.4 Model Provision and Accessibility

- Analysis of the clinical and economic value of a product is fundamental to the process.
- Explanatory statement if a model is not provided

- Strongly recommend delivery of a model to users for use on their own time
- Concerns about ‘unsupervised’ use of model should be addressed.
- Strongly discourage limited access to a model as this raises significant barriers to model validation.
- Models should be user-friendly software, spreadsheet software is recommended
- All inputs must be modifiable
- All formulas/equations driving the model should be accessible within the model
- In cases where complex software or modeling approaches are used, key risk equations that drive the model must be provided in text format and part of the model

5.0 Other Supporting Evidence

5.1 Summarizing Other Relevant Evidence (2 page maximum per study) – Summaries of other relevant supporting evidence including, but not limited to, retrospective studies that provide information not available from clinical trials, meta-analyses and systematic reviews of clinical, quality of life and economic outcomes, comparative observational studies of effectiveness and harms, assessments of adherence or persistence studies of patient preference, predictive risk models, and indirect comparisons of clinical benefit using Bayesian or other appropriate methods, whether published or not.

5.1.1 Published and Unpublished Studies Supporting Labeled and Off-Label Indications – Summaries of relevant economic studies should include the following:

- Definition of economic endpoints (mean overall cost, cancer-related cost, \$/LYG, \$/QALY, etc.) including references for standard of care costs
- Data sources for economic endpoints
- Statistical methods/math used to calculate endpoints
- Modeling methodology (if applicable)
- Sensitivity analysis (if applicable)
- Unpublished data: Provide as much detail as can be disclosed.

5.1.2 Evidence Table Spreadsheets – Information from all studies described in this section should be summarized in evidence tables (spreadsheet format). Include negative or null findings as well as positive findings.