H-120.988 Patient Access to Treatments Prescribed by Their Physicians

The AMA confirms its strong support for the autonomous clinical decision-making authority of a physician and that a physician may lawfully use an FDA approved drug product or medical device for an unlabeled indication when such use is based upon sound scientific evidence and sound medical opinion; and affirms the position that, when the prescription of a drug or use of a device represents safe and effective therapy, third party payers, including Medicare, should consider the intervention as reasonable and necessary medical care, irrespective of labeling, should fulfill their obligation to their beneficiaries by covering such therapy, and be required to cover appropriate "off-label" uses of drugs on their formulary. The AMA recommends the following:

Prescribing and Reimbursement for FDA-Approved Drugs and Devices for Unlabeled Uses

(1) Our AMA reaffirms the following policies: (a) A physician may lawfully use an FDA-approved drug product or medical device for an unlabeled indication when such use is based upon sound scientific evidence and sound medical opinion (Policy H-120.988); (b) When the prescription of a drug or use of a device represents safe and effective therapy, third party payers, including Medicare, should consider the intervention as reasonable and necessary medical care, irrespective of labeling, and should fulfill their obligation to their beneficiaries by covering such therapy (Policy H-120.988); and (c) Our AMA encourages the use of three compendia (AMA's Drug Evaluations*; United States Pharmacopeia-Drug Information, Volume I*; and American Hospital Formulary Service-Drug Information) and the peer-reviewed literature for determining the medical acceptability of unlabeled uses (Policy H-165.896, #15). (*These two compendia currently are being merged as the result of an alliance between the American Medical Association and the United States Pharmacopeia.)

Dissemination of Information about Unlabeled Uses of Drugs and Devices by Manufacturers

(2) Our AMA strongly supports the important need for physicians to have access to accurate and unbiased information about unlabeled uses of drugs and devices, while ensuring that manufacturer-sponsored promotions remain under FDA regulation. (3) Our AMA supports the dissemination of independently derived scientific information about unlabeled uses by manufacturers to physicians, if the independent information is provided in its entirety, is not edited or altered by the manufacturer, and is clearly distinguished from manufacturer-sponsored materials. Dissemination of information by manufacturers to physicians about unlabeled uses can be supported under the following conditions: (a) Reprints of independently derived articles from reputable, peer-reviewed journals that meet the following criteria: (i) The article should be peer reviewed and published in accordance with the regular peer review procedure of the journal in which it is published; (ii) The reprint should be from a peer-reviewed journal that both has an editorial board and utilizes experts to review and objectively select, reject, or provide comments about proposed articles; such experts should have demonstrated expertise in the subject of the article under review, and be independent from the journal; (iii) The journal is recognized to be of national scope and reputation, as defined by an advisory panel to the FDA; among its members, this advisory panel should have representatives from national medical societies; (iv) The journal must be indexed in the Index Medicus of the National Library of Medicine; (v) The journal must have and adhere to a publicly stated policy of full disclosure of any conflicts of interest or biases for all authors or contributors; (vi) When the subject of the article is an unlabeled use, or the article contains other information that is different from approved labeling, the industry sponsor disseminating the reprint must disclose that the reprint includes information that has not been approved by the FDA and attach a copy of the FDA-approved professional labeling with the reprint; (vii) If financial support for the study and/or the author(s) was provided by the industry

sponsor disseminating the article, and this is not already stated in the article, then this information should be clearly disclosed with the reprint. (b) Reprints of monographs or chapters from the three compendia (AMA's Drug Evaluations; United States Pharmacopeia-Drug Information, Volume I; and American Hospital Formulary Service-Drug Information) named in federal statutes for determining the medical acceptability of unlabeled uses, provided: (i) The monograph or chapter is reprinted in its entirety by the publisher of the compendia, and the reprints are then sent to the requesting industry sponsor; (ii) The reprints are not altered in any way by the industry sponsor; (iii) The industry sponsor disseminating the reprint discloses that the reprint includes information that has not been approved by the FDA and attaches a copy of the FDA-approved professional labeling with the reprint. (c) Complete textbooks that meet the following criteria: (i) The reference text should not have been written, edited, excerpted, or published specifically for, or at the request of, a drug, device, or biologic firm; when financial support is provided by a drug, device, or biologic firm, it should be disclosed clearly in the textbook; (ii) The content of the reference text should not have been edited or significantly influenced by a drug, device, or biologic firm, or agent thereof; (iii) The reference text should be generally available for sale in bookstores or other distribution channels where similar books are normally available and should not be distributed only or primarily through drug, device, or biologic firms; (iv) The reference text should not focus primarily on any particular drug(s), device(s), or biologic(s) of the disseminating company, nor should it have a significant focus on unapproved uses of drug(s), device(s), or biologic(s) marketed or under investigation by the firm supporting the dissemination of the text; (v) Specific product information (other than the approved package insert) should not be physically appended to the reference text. (d) Manufacturers should report to the FDA and share with all physicians any proprietary information that a drug is ineffective or unsafe when used for a specific unlabeled indication. (e) Continuing medical education (CME) activities: (i) The FDA should continue to support principles in the FDA Draft Policy Statement on Industry-Supported Scientific and Educational Activities (Fed. Reg. 1992;57:56412-56414), which acknowledges the importance of relying on the professional health-care communities, rather than the Agency, to monitor independent provider activities; and (ii) The FDA should continue a policy of regulatory deference for industry-supported CME activities conducted by organizations accredited by the Accreditation Council for Continuing Medical Education (ACCME), state medical societies, specialty societies, and the American Academy of Family Physicians (AAFP), that follow the Essentials and Standards of the ACCME and that may be certified for AMA PRA credit under the auspices of the American Medical Association Physician's Recognition Award program. (4) Physicians have the responsibility to interpret and put into context information received from any source, including pharmaceutical manufacturers, before making clinical decisions (e.g., prescribing a drug for an unlabeled use).Improving the Supplemental New Drug Application (SNDA) Process (5) Our AMA strongly supports the addition to FDA-approved labeling those uses of drugs for which safety and efficacy have been demonstrated. (6) Our AMA encourages the US Congress, the FDA, pharmaceutical manufacturers, the United States Pharmacopeia, patient organizations, and medical specialty societies to work together to ensure that Supplemental New Drug Applications (SNDAs) for new indications (efficacy supplements), including those for uses in special populations (e.g., pediatrics), are submitted and acted upon in a timely manner. Specific recommendations include: (a) User fee legislation should be re-authorized to ensure that the FDA has the necessary resources to act on all efficacy supplements within 6 months of submission; (b) The SNDA process should be streamlined as much as possible (e.g., basing review decisions on already published literature), without compromising the requirements for substantial evidence of efficacy and safety; (c) Legislation should be enacted that provides extensions of marketing exclusivity for the product to manufacturers who submit and gain FDA approval of efficacy supplements, including mechanisms both to provide greater reward when the new indication is for a life-threatening disease (with limited or no alternatives), an orphan disease, or for a special population (e.g., pediatrics), and to prevent inappropriate use of the system by manufacturers (e.g., place a limit on total length of extended marketing exclusivity); (d) For drugs no longer under patent and for which generic versions are available, the FDA, other governmental agencies (e.g., the National Institutes of Health), the pharmaceutical industry, the United States Pharmacopeia, patient organizations, and medical specialty societies should discuss and mutually agree on alternative mechanisms to ensure that efficacy supplements will

be submitted to and acted upon by the FDA in a timely manner; and (e) Pharmaceutical manufacturers are urged to seek FDA approval for pediatric uses through the FDA's 1994 regulation that allows approval of pediatric uses based on adult efficacy studies (where the course of the disease and the effects of the drug are sufficiently similar in both populations) and additional information for pediatric use, usually pharmacokinetic studies for determination of dosage (Fed. Reg. 1994:59:64240-64250).

Encouraging Clinical Research in Pediatrics

(7) Our AMA urges pharmaceutical manufacturers and the FDA to work with the American Academy of Pediatrics and experts in pediatric medicine to identify those investigational drugs that would have pediatric indications and set up a mechanism to ensure that necessary pediatric clinical studies are completed prior to submission of NDAs for approval of these drug products. Legislation should be enacted that provides extensions of marketing exclusivity for the product to manufacturers who complete pediatric studies that lead to pediatric labeling (Res. 30, A-88; Reaffirmed: BOT Rep. 53, A-94; Reaffirmed and Modified by CSA Rep. 3, A-97; Reaffirmed and Modified by Res. 528, A-99; Reaffirmed: CMS Rep. 8, A-02; Reaffirmed: CMS Rep. 6, A-03; Modified: Res. 517, A-04; Reaffirmation I-07; Reaffirmed: Res. 819, I-07)