

AMERICAN MEDICAL ASSOCIATION HOUSE OF DELEGATES

Resolution: 809  
(I-16)

Introduced by: Medical Student Section

Subject: Addressing the Exploitation of Restricted Distribution Systems by  
Pharmaceutical Manufacturers

Referred to: Reference Committee J  
(Candace E. Keller, Chair)

1 Whereas, A litany of prescription drugs have recently experienced significant price increases  
2 shortly after changes of ownership, such as colchicine, Thiola, Daraprim, and Makena, which in  
3 the past five years have seen price increases of 2000%, 2000%, 5000%, and 15,000%,  
4 respectively;<sup>1,2,3,4,5,6</sup> and

5  
6 Whereas, The mechanism by which companies are able to implement such price hikes involves,  
7 in part, the transition from a traditional wholesaler-based supply chain model to a “restricted”,  
8 “controlled”, or “closed” distribution system at the discretion of the manufacturer;<sup>7,8</sup> and

9  
10 Whereas, A restricted distribution system is a tightly-controlled supply chain model in which a  
11 drug is only available to patients via specific specialty pharmacies, enabling drug manufacturers  
12 to stringently control the distribution of their products; and

13  
14 Whereas, Per the 1984 Hatch-Waxman Act and current FDA guidelines, in order for a generic  
15 manufacturer to receive FDA approval to sell a generic variant of a brand-name drug, it must  
16 demonstrate bioequivalence, necessitating the purchase of non-trivial quantities of the brand-  
17 name drug, a process that is greatly complicated by restricted distribution;<sup>9,10</sup> and

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<sup>1</sup> Langreth, R. and Koons, C. (2015) 2,000% Drug Price Surge Is a Side Effect of FDA Safety Program. Bloomberg Business, Available at: <http://www.bloomberg.com/news/articles/2015-10-06/2-000-drug-price-surge-is-a-side-effect-of-fda-safety-program>

<sup>2</sup> Marketed Unapproved Drugs Compliance Policy Guide § 440.100 Marketed New Drugs Without Approved NDAs or ANDAs. Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070290.pdf>

<sup>3</sup> Brozak, S. (2014) Retrophin, Gilead, And Our Healthcare Values. Forbes, Available at: <http://www.forbes.com/sites/stephenbrozak/2014/09/12/retrophin-gilead-and-our-healthcare-values/#2299c6f9fca4>

<sup>4</sup> Patel Y, Rumore MM. Hydroxyprogesterone caproate injection (makena) one year later: to compound or not to compound that is the question. P T. 2012;37(7):405-11.

<sup>5</sup> Stobbe, M. (2011) Premature Labor Drug Spikes from \$10 to \$1,500. NBC News, Available at: <http://www.nbcnews.com/id/41994697/ns/health-pregnancy/t/premature-labor-drug-spikes/>

<sup>6</sup> Lorenzetti, L. (2015) This 62-Year-Old Drug Just Got 5000% More Expensive. Fortune, Available at: <http://fortune.com/2015/09/21/turing-pharmaceuticals-drug-prices-daraprim/>

<sup>7</sup> Carrier, M and Kesselheim A. (2015) The Daraprim Price Hike and a Role for Antitrust. Health Affairs Blog, Available at: <http://healthaffairs.org/blog/2015/10/21/the-daraprim-price-hike-and-a-role-for-antitrust/>

<sup>8</sup> Mahoney, M. (2015) New Pyrimethamine Dispensing Program: What Pharmacists Should Know. Pharmacy Times, Available at: <http://www.pharmacytimes.com/contributor/monica-v-golik-mahoney-pharmd-bcps-aq-id/2015/07/new-pyrimethamine-dispensing-program-what-pharmacists-should-know#sthash.lruZY1k5.dpuf>

<sup>9</sup> Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA. (2013). United States Food and Drug Administration. Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM377465.pdf>

<sup>10</sup> Tucker D., Wells G., and Sheer, M. (2014) REMS: The Next Pharmaceutical Enforcement Priority? Antitrust. Available at: [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=2410950](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2410950)

1 Whereas, Often, though not always, a restricted distribution system implemented by FDA  
2 mandate as part of a Risk Evaluation & Mitigation Strategy (REMS) when the drug in question is  
3 associated with considerable health risks or other regulatory or clinical concerns such as  
4 counterfeiting and abuse;<sup>7,8,11,12,13,14</sup> and

5  
6 Whereas, Restricted distribution systems, even when implemented by FDA mandate per a  
7 REMS, are being exploited to block generic entry into the market by making it virtually  
8 impossible for generic manufacturers to obtain the necessary materials to perform  
9 bioequivalence testing, and the potential for exploitation is even greater when restricted  
10 distribution is implemented unilaterally at the manufacturer's discretion;<sup>10,15,16,17</sup> and

11  
12 Whereas, Provisions of the Food and Drug Administration Amendments Act of 2007 sought to  
13 address circumstances in which REMS can pose barriers to generic entry, but "it remains  
14 unclear whether the FDA even has any authority to enforce the prohibition against companies  
15 using a REMS to block generic entry" and the FDA has stated that it lacks an enforcement  
16 mechanism;<sup>10,12,14,15,16</sup> and

17  
18 Whereas, The FDA has a backlog of some 4,300 generic drug applications pending approval as  
19 of December 2015 and the median approval time rose from 27 months in 2010 to 36 months in  
20 2013, despite the infusion of \$300 million from generic manufacturers in 2012 per the Generic  
21 Drug User Fee Amendments, which was intended to facilitate faster approval;<sup>18,19,20</sup> and

22  
23 Whereas, On March 1, 2016, Senator Susan Collins introduced S. 2615 "Increasing Competition  
24 in Pharmaceuticals Act", which directs the FDA to act within 150 days on generic drug  
25 applications when there is only one competing product available, and creates a "generic priority  
26 review voucher" program to speed approval of other generics;<sup>21,22</sup> and

27  
28 Whereas, Existing AMA policy seeks to address "the already high and escalating costs of  
29 generic prescription drugs" (H-110.988) while recognizing their cost-saving potential (H-  
30 125.984); therefore be it

31  
32 **RESOLVED**, That our American Medical Association advocate with interested parties for  
33 legislative or regulatory measures that require prescription drug manufacturers to seek Federal  
34 Drug Administration and Federal Trade Commission approval before establishing a restricted  
35 distribution system (New HOD Policy); and be it further

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<sup>11</sup> Kirschenbaum BE. Specialty pharmacies and other restricted drug distribution systems: financial and safety considerations for patients and health-system pharmacists. *Am J Health Syst Pharm.* 2009;66(24 Suppl 7):S13-20.

<sup>12</sup> Battaglia, L. (2013) Risky Conduct with Risk Mitigation Strategies? The Potential Antitrust Issues Associated with REMS. *Antitrust Healthcare Chronicle*, Available at: <http://www.hlregulation.com/files/2013/10/Lauren-Battaglia-article1.pdf>

<sup>13</sup> Oral Cancer Agents Are Changing The Distribution Channel. (2006) *Oncology Business Review*, Available at: <https://obroncology.com/journal-current-dtl.php?recordID=8>

<sup>14</sup> Risk evaluation and mitigation strategies, 21 U.S.C. § 355-1 (2010).

<sup>15</sup> Tucker D., Wells G., and Sheer, M. (2014) REMS: The Next Pharmaceutical Enforcement Priority? *Antitrust*. Available at: [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=2410950](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2410950)

<sup>16</sup> Fabish, A. (2015). REMS Abuse And Antitrust Injury: Round Peg, Square Hole. *Law360*. Available at: <http://www.law360.com/articles/723053/rem-abuse-and-antitrust-injury-round-peg-square-hole>

<sup>17</sup> Fabish, A. (2015). Why REMS Abuse Doesn't Belong In Antitrust Litigation. *Law360*. Available at: <http://www.law360.com/articles/645875/why-rem-abuse-doesn-t-belong-in-antitrust-litigation>

<sup>18</sup> Herrick, D. (2015) What Is Increasing the Cost of Generic Drugs? Part I: The Supply Chain. *National Center for Policy Analysis*, Available at: <http://www.ncpa.org/pdfs/st371.pdf>

<sup>19</sup> Kaplan, S. (2015) One Reason for High Drug Prices: a Huge Backlog of Unapproved Generic Drugs. *STAT*, Available at: <http://www.statnews.com/2015/12/29/generic-drugs-backlog/>

<sup>20</sup> Barlas S. Generic prices take flight: the FDA is struggling to ground them. *P T.* 2014;39(12):833-45.

<sup>21</sup> To Increase Competition in the Pharmaceutical Industry, S. S. 2615, 114th Cong. (2016). Print. Available at: <https://www.congress.gov/bill/114th-congress/senate-bill/2615/text>

<sup>22</sup> Brennan, Zachary. (2016) More Competition: Senator Proposes Priority Reviews for Some Generics, New Voucher Program. *Regulatory Affairs Professional Society*. Available at: <http://www.raps.org/Regulatory-Focus/News/2016/03/03/24466/More-Competition-Senator-Proposes-New-Priority-Reviews-for-Some-Generics-New-Voucher-Program/>

- 1 RESOLVED, That our AMA support the mandatory provision of samples of approved out-of-  
2 patent drugs upon request to generic manufacturers seeking to perform bioequivalence assays  
3 (New HOD Policy); and be it further  
4  
5 RESOLVED, That our AMA advocate with interested parties for legislative or regulatory  
6 measures that expedite the FDA approval process for generic drugs, including but not limited to  
7 application review deadlines and generic priority review voucher programs. (New HOD Policy)

Fiscal Note: Not yet determined

Received: 09/29/16

### RELEVANT AMA POLICY

**Cost of New Prescription Drugs H-110.998** - Our AMA urges the pharmaceutical industry to exercise reasonable restraint in the pricing of drugs.

Res. 112, I-89 Reaffirmed: Res. 520, A-99 Reaffirmed: CSAPH Rep. 1, A-09 Reaffirmed in lieu of Res. 229, I-14

**Reducing Prescription Drug Prices D-110.993** - Our AMA will (1) continue to meet with the Pharmaceutical Research and Manufacturers of America to engage in effective dialogue that urges the pharmaceutical industry to exercise reasonable restraint in the pricing of drugs; and (2) encourage state medical associations and others that are interested in pharmaceutical bulk purchasing alliances, pharmaceutical assistance and drug discount programs, and other related pharmaceutical pricing legislation, to contact the National Conference of State Legislatures, which maintains a comprehensive database on all such programs and legislation.

CMS Rep. 3, I-04 Modified: CMS Rep. 1, A-14 Reaffirmation A-14 Reaffirmed in lieu of Res. 229, I-14

**Inappropriate Extension of Patent Life of Pharmaceuticals D-110.994** - Our AMA will continue to monitor the implementation of the newly-enacted reforms to the Hatch-Waxman law to see if further refinements are needed that would prevent inappropriate extension of patent life of pharmaceuticals, and work accordingly with Congress and the Administration to ensure that AMA policy concerns are addressed.

BOT Rep. 21, A-04 Reaffirmed: BOT Rep. 19, A-14

**The Evolving Culture of Drug Safety in the United States: Risk Evaluation and Mitigation Strategies (REMS) H-100.961** - Our AMA urges that: (1) The Food and Drug Administration (FDA) issue a final industry guidance on Risk Evaluation and Mitigation Strategies (REMS) with provisions that: (a) require sponsors to consult with impacted physician groups and other key stakeholders early in the process when developing REMS with elements to assure safe use (ETASU); (b) establish a process to allow for physician feedback regarding emerging issues with REMS requirements; (c) clearly specify that sponsors must assess the impact of ETASU on patient access and clinical practice, particularly in underserved areas or for patients with serious and life threatening conditions, and to make such assessments publicly available; and (d) conduct a long-term assessment of the prescribing patterns of drugs with REMS requirements. (2) The FDA ensure appropriate Advisory Committee review of proposed REMS with ETASU before they are finalized as part of the premarket review of New Drug Applications, and that the Drug Safety and Risk Management Advisory Committee fulfills this obligation for drugs that are already on the market and subject to REMS because of new safety information. (3) To the extent practicable, a process is established whereby the FDA and sponsors work toward standardizing procedures for certification and enrollment in REMS programs, and the common

definitions and procedures for centralizing and standardizing REMS that rely on ETASU are developed. (4) REMS-related documents intended for patients (e.g., Medication Guides, acknowledgment/consent forms) be tested for comprehension and be provided at the appropriate patient literacy level in a culturally competent manner. (5) The Food and Drug Administration (FDA) issue a final industry guidance on Risk Evaluation and Mitigation Strategies (REMS) with provisions that: (a) urge sponsors to consult with impacted physician groups and other key stakeholders early in the process when developing REMS with elements to assure safe use (ETASU); (b) establish a process to allow for physician feedback regarding emerging issues with REMS requirements; and (c) recommend that sponsors assess the impact of ETASU on patient access and clinical practice, particularly in underserved areas or for patients with serious and life threatening conditions, and to make such assessments publicly available. (6) The FDA, in concert with the pharmaceutical industry, evaluate the evidence for the overall effectiveness of REMS with ETASU in promoting the safe use of medications and appropriate prescribing behavior. (7) The FDA ensure appropriate Advisory Committee review of proposed REMS with ETASU before they are finalized as part of the premarket review of New Drug Applications, and that the Drug Safety and Risk Management Advisory Committee fulfills this obligation for drugs that are already on the market and subject to REMS because of new safety information. (8) To the extent practicable, a process is established whereby the FDA and sponsors work toward standardizing procedures for certification and enrollment in REMS programs, and the common definitions and procedures for centralizing and standardizing REMS that rely on ETASU are developed. (9) REMS-related documents intended for patients (e.g., Medication Guides, acknowledgment/consent forms) be tested for comprehension and be provided at the appropriate patient literacy level in a culturally competent manner. (10) The FDA solicit input from the physician community before establishing any REMS programs that require prescriber training in order to ensure that such training is necessary and meaningful, requirements are streamlined and administrative burdens are reduced.

CSAPH Rep. 8, A-10 Reaffirmed: Res. 917, I-10 Appended: CSAPH Rep. 3, I-12

**Pharmaceutical Cost H-110.987** - 1. Our AMA encourages Federal Trade Commission (FTC) actions to limit anticompetitive behavior by pharmaceutical companies attempting to reduce competition from generic manufacturers through manipulation of patent protections and abuse of regulatory exclusivity incentives. 2. Our AMA encourages Congress, the FTC and the Department of Health and Human Services to monitor and evaluate the utilization and impact of controlled distribution channels for prescription pharmaceuticals on patient access and market competition. 3. Our AMA will monitor the impact of mergers and acquisitions in the pharmaceutical industry. 4. Our AMA will continue to monitor and support an appropriate balance between incentives based on appropriate safeguards for innovation on the one hand and efforts to reduce regulatory and statutory barriers to competition as part of the patent system. 5. Our AMA encourages prescription drug price and cost transparency among pharmaceutical companies, pharmacy benefit managers and health insurance companies. 6. Our AMA supports legislation to require generic drug manufacturers to pay an additional rebate to state Medicaid programs if the price of a generic drug rises faster than inflation. 7. Our AMA supports legislation to shorten the exclusivity period for biologics. 8. Our AMA will convene a task force of appropriate AMA Councils, state medical societies and national medical specialty societies to develop principles to guide advocacy and grassroots efforts aimed at addressing pharmaceutical costs and improving patient access and adherence to medically necessary prescription drug regimens. 9. Our AMA will generate an advocacy campaign to engage physicians and patients in local and national advocacy initiatives that bring attention to the rising price of prescription drugs and help to put forward solutions to make prescription drugs more affordable for all patients, and will report back to the House of Delegates regarding the progress of the drug pricing advocacy campaign at the 2016 Interim Meeting.

CMS Rep. 2, I-15

**Controlling the Skyrocketing Costs of Generic Prescription Drugs H-110.988** - 1. Our American Medical Association will work collaboratively with relevant federal and state agencies, policymakers and key stakeholders (e.g., the U.S. Food and Drug Administration, the U.S. Federal Trade Commission, and the Generic Pharmaceutical Association) to identify and promote adoption of policies to address the already high and escalating costs of generic prescription drugs. 2. Our AMA will advocate with interested parties to support legislation to ensure fair and appropriate pricing of generic medications, and educate Congress about the adverse impact of generic prescription drug price increases on the health of our patients. 3. Our AMA encourages the development of methods that increase choice and competition in the development and pricing of generic prescription drugs. 4. Our AMA supports measures that increase price transparency for generic prescription drugs.  
Sub. Res. 106, A-15 Reaffirmed: CMS 2, I-15

**Study of Actions to Control Pharmaceutical Costs H-110.992** - Our AMA will monitor the relationships between pharmaceutical benefits managers and the pharmaceutical industry and will strongly discourage arrangements that could cause a negative impact on the cost or availability of essential drugs.  
Sub. Res. 114, A-01 Reaffirmed: Res. 533, A-03 Reaffirmed: CMS Rep. 4, A-13 Reaffirmed in lieu of Res. 229, I-14 Reaffirmed: CMS 2, I-15

**Cost of Prescription Drugs H-110.997** - Our AMA: (1) supports programs whose purpose is to contain the rising costs of prescription drugs, provided that the following criteria are satisfied: (a) physicians must have significant input into the development and maintenance of such programs; (b) such programs must encourage optimum prescribing practices and quality of care; (c) all patients must have access to all prescription drugs necessary to treat their illnesses; (d) physicians must have the freedom to prescribe the most appropriate drug(s) and method of delivery for the individual patient; and (e) such programs should promote an environment that will give pharmaceutical manufacturers the incentive for research and development of new and innovative prescription drugs;(2) reaffirms the freedom of physicians to use either generic or brand name pharmaceuticals in prescribing drugs for their patients and encourages physicians to supplement medical judgments with cost considerations in making these choices;(3) encourages physicians to stay informed about the availability and therapeutic efficacy of generic drugs and will assist physicians in this regard by regularly publishing a summary list of the patient expiration dates of widely used brand name (innovator) drugs and a list of the availability of generic drug products;(4) encourages expanded third party coverage of prescription pharmaceuticals as cost effective and necessary medical therapies;(5) will monitor the ongoing study by Tufts University of the cost of drug development and its relationship to drug pricing as well as other major research efforts in this area and keep the AMA House of Delegates informed about the findings of these studies;(6) encourages physicians to consider prescribing the least expensive drug product (brand name or FDA A-rated generic); and(7) encourages all physicians to become familiar with the price in their community of the medications they prescribe and to consider this along with the therapeutic benefits of the medications they select for their patients.  
BOT Rep. O, A-90 Sub. Res. 126 and Sub. Res. 503, A-95 Reaffirmed: Res. 502, A-98 Reaffirmed: Res. 520, A-99 Reaffirmed: CMS Rep. 9, I-99 Reaffirmed: CMS Rep.3, I-00 Reaffirmed: Res. 707, I-02 Reaffirmation A-04 Reaffirmed: CMS Rep. 3, I-04 Reaffirmation A-06 Reaffirmed in lieu of Res. 814, I-09 Reaffirmed in lieu of Res. 201, I-11

**Generic Drugs H-125.984** - Our AMA believes that: (1) Physicians should be free to use either the generic or brand name in prescribing drugs for their patients, and physicians should supplement medical judgments with cost considerations in making this choice. (2) It should be recognized that generic drugs frequently can be less costly alternatives to brand-name

products. (3) Substitution with Food and Drug Administration (FDA) "B"-rated generic drug products (i.e., products with potential or known bioequivalence problems) should be prohibited by law, except when there is prior authorization from the prescribing physician. (4) Physicians should report serious adverse events that may be related to generic substitution, including the name, dosage form, and the manufacturer, to the FDA's MedWatch program. (5) The FDA, in conjunction with our AMA and the United States Pharmacopoeia, should explore ways to more effectively inform physicians about the bioequivalence of generic drugs, including decisional criteria used to determine the bioequivalence of individual products. (6) The FDA should fund or conduct additional research in order to identify the optimum methodology to determine bioequivalence, including the concept of individual bioequivalence, between pharmaceutically equivalent drug products (i.e., products that contain the same active ingredient(s), are of the same dosage form, route of administration, and are identical in strength). (7) The Congress should provide adequate resources to the FDA to continue to support an effective generic drug approval process.

CSA Rep. 6, A-02 Reaffirmed: CSAPH Rep. 2, A-07 Reaffirmation A-08 Reaffirmation A-09 Reaffirmed in lieu of Res. 525, A-10 Reaffirmed in lieu of Res. 224, I-14

**Cost Sharing Arrangements for Prescription Drugs H-110.990** - Our AMA: 1. believes that cost-sharing arrangements for prescription drugs should be designed to encourage the judicious use of health care resources, rather than simply shifting costs to patients; 2. believes that cost-sharing requirements should be based on considerations such as: unit cost of medication; availability of therapeutic alternatives; medical condition being treated; personal income; and other factors known to affect patient compliance and health outcomes; and 3. supports the development and use of tools and technology that enable physicians and patients to determine the actual price and out-of-pocket costs of individual prescription drugs prior to making prescribing decisions, so that physicians and patients can work together to determine the most efficient and effective treatment for the patient's medical condition.

CMS Rep. 1, I-07 Reaffirmation A-08 Reaffirmed: CMS Rep. 1, I-12 Reaffirmed in lieu of Res. 105, A-13

**Generic Changes in Medicare (Part D) Plans D-330.911** - 1. Our AMA will investigate the incidence and reasoning behind the conversion of one generic drug to another generic drug of the same class in Medicare Advantage drug plans. 2. Our AMA will request the Centers for Medicare & Medicaid Services to ensure that pharmaceutical vendors, when they do ask for generic transitions of drugs, list the drugs they believe are more cost effective along with their tier price and alternative drug names.

Res. 124, A-14