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The Gerontological Society of America (GSA) is pleased to present this statement for the record in response to [Docket No. FDA–2014–N–0202] Over-The-Counter Drug Monograph System—Past, Present, and Future.

GSA is the largest multidisciplinary professional membership organization of researchers studying all facets of aging on a national and international scale. The Society’s members include physicians, nurses, biologists, psychologists, social workers, economists, health policy experts and others interested in expanding scientific knowledge related to aging. Because of the breadth and depth of our members’ interests and scholarship in gerontology and geriatric practice, GSA’s strengths in this knowledge domain may be of benefit to FDA in obtaining information and comments on the above-referenced process, especially as such changes concern older adults’ unique needs. The following comments have been developed with input from GSA’s OTC Sleep Aids and Sleep Health of Older Adults multidisciplinary workgroup of subject matter experts in medicine, pharmacy, nursing, public health, and research.

GSA’s comments will focus on the FDA’s process that seeks to address emerging safety concerns with OTC medications for an aging society. One out of every 9 Americans is aged 65 years or older—a population that is greater than the number of inhabitants of New York, London, and Moscow combined. The aging baby boomers are increasing the proportion of older adults in the United States with 10,000 people turning 65 years old every day. Available data on over-the-counter (OTC) medication-taking behaviors of older adults describe the extent of medication use. For example, while older adults comprise 13% of the U.S. population, they account for 34% of prescription drug use and 30% of nonprescription or OTC medication use.

The 2008 National Social Life, Health, and Aging Project examined the prevalence of both OTC and prescription medication use among adults aged 57 to 85 years old. Results of the survey showed that 81% of the respondents took at least one prescription medication (29% took five or more prescription medications concurrently); 42% used at least one OTC medication; and 49% used a dietary supplement. Of those taking a prescription medication, 46% also took an OTC medication.
The October 2010 Pharmacy Today “White paper on the benefits of OTC medicines in the United States” reported on the important role of OTC medicines in the treatment of many conditions citing accessibility and convenience as important features. The Center for Drug Evaluation and Research oversees OTC drugs and ensures they generally have benefits that outweigh risks, low potential for misuse and abuse; consumers can use them for self-diagnosed condition; they can be adequately labeled; health practitioners are not needed for their safe and effective use. OTC products are widely recommended by physicians and their use may be endorsed in clinical practice guidelines as “first line” therapy. GSA recognizes the positive impact and benefits that OTC products have in older adults, as well as the economic implications to the healthcare system, payers, consumers, caregivers, and communities.

Age-related factors can impact a drug’s safety and efficacy. The Federal Register notice details important and relevant information about drug metabolism and action in infants and children. Similarly, research and knowledge of aging-related changes also have evolved considerably since the monograph system was established in the early 1970s. Among these changes are reductions in liver and kidney function, which affect a drug’s absorption and elimination; memory impairments, hearing loss, and visual difficulties that can make it difficult to understand and remember medication instructions; declines in weight, loss of body fluid, and increased percentage of body fat, which can alter the way drugs are distributed and concentrated in the body.²

The older adult population present unique challenges for those seeking to develop and market OTC medications to improve the health and quality of life of older adults; a modernized OTC review process must be responsive also to these important needs, and GSA shares FDA’s concerns that the current OTC Monograph system may be inadequate to address these needs. To illustrate these issues, we focus on sleep as an example.

Sleep, like nutrition and exercise, is a key determinant of health and well-being. Sleep is a basic human requirement that affects endocrine, metabolic, neurological, and cognitive functions that are critical to health.

According to the Centers for Disease Control and Prevention, 25% of U.S. adults report insufficient sleep or rest at least 15 out of every 30 days.⁴ Despite multifactorial reasons for inadequate sleep, many adults who report disturbed sleep suffer from insomnia—unsatisfactory sleep that affects daytime functioning in an individual who has adequate opportunity to sleep.⁵ Patients with insomnia may experience difficulty either falling asleep or staying asleep.

Among those who experience disturbed sleep, an estimated 50 million to 70 million Americans have chronic insomnia, a sleep disruption occurring at least 3 times a week and lasting for more than 1 month. In addition to hindering daily functioning, chronic insomnia has been associated with a wide range of harmful health effects, including an increased risk of hypertension, diabetes, obesity, depression, heart attack, stroke, and pain.⁵,⁶
Recent data from the Kantar Health March 2013 National Health and Wellness Survey found that OTC sleep aid use among adults older than 60 years of age is extensive.\(^7\) Among these individuals:

- Fifteen percent to 18% reported using OTC sleep aids alone; about 3% used OTCs combined with herbs; and about 15% to 18% took OTCs in combination with prescription sleep aids.
- More than 70% reported taking OTC pain and sleep combination products, with single-molecule product use at nearly 30%.
- Of the respondents aged 60 to 75 and older who reported taking OTC sleep agents, approximately 40% also currently take one or more anticholinergic medications. (It is important to remember that all currently available OTC sleep aids have anticholinergic properties and are associated with cognitive impairments, especially in older adults.)

The risks and benefits of OTC sleep aids for the treatment of disturbed sleep in older adults have not been examined in randomized controlled trials. Nevertheless, a substantial body of data has identified risks associated with these products and several authoritative sources caution against their use.\(^8\) Efforts to improve medication-use behaviors among older adults include use of the Beers Criteria for potentially inappropriate medication use in older adults. Originally developed by Mark H. Beers, MD, a geriatrician, the Beers Criteria were published in 1991. The criteria were updated in 1997, in 2003, and most recently in 2012. The 2012 version is the first update to include OTC medications such as first-generation antihistamines, including diphenhydramine (the most common active ingredient in OTC sleep aids). According to the Beers Criteria, first-generation antihistamines should generally be avoided in older adults due to their anticholinergic activity. Regarding these agents, the criteria state: “Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; greater risk of confusion, dry mouth, constipation, and other anticholinergic effects and toxicity.” (The criteria do note that use of diphenhydramine in special situations, such as acute treatment of severe allergic reaction, may be appropriate.)

Given older adults’ high prevalence of reported sleep problems, they commonly use medications to help them sleep. Therefore, it is critical to consider age-related issues in the OTC drug development, review, and approval process. The important issues to consider are:

1. Does the drug show age-related differences in kinetics? If so, do older adults need different doses? This is generally done with Rx medications? Are the changes in kinetics associated with adverse events, such as drug hangovers?
2. Older adults typically take multiple medications and, therefore, are more susceptible to pharmacodynamic drug interactions. As such, additional pharmacodynamic studies are needed for older adults.
3. Are there medication-related adverse events that may contribute to falling risk, cognitive impairment, or other anticholinergic side effects?

In conclusion, The Gerontological Society of America suggests FDA consider OTC medication review and labeling that would address and be responsive to evolving science specific to safety.
risks of medication use associated with the aging process. While OTC medications to aid sleep were used as an example in today’s comments, GSA would welcome an opportunity to provide additional input and guidance to ensure that a modernized OTC drug review process considers aging-related factors such as dosing, labeling, and packaging. In addition, GSA has a number of special publications in this area, which are available at www.geron.org/otc.

Thank you,
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References