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## Direct-to-Consumer Advertising of Alzheimer's Disease Drugs

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*(Article begins on next page)*

# **Direct-to-Consumer Advertising of Alzheimer's Disease Drugs**

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Course Paper for Food and Drug Law

## **Abstract**

Use of direct-to-consumer (DTC) advertising by pharmaceutical manufacturers has skyrocketed in the past few decades as patients demand more information on drugs and the FDA has gotten more relaxed in its regulation of such marketing. In particular, television advertisements for prescription drugs for chronic conditions have dramatically increased. This paper will analyze the use of DTC advertising for prescription drugs for Alzheimer's disease, a debilitating disease which can last for more than a decade before it leads to death. The paper will start with a history of DTC advertising and the FDA's regulation of such advertisements. It will then proceed to analyze issues of DTC advertising which are particularly pertinent for Alzheimer's disease, with an in-depth look at Aricept, one FDA-approved drug for Alzheimer's. The paper will conclude with suggestions for further studies in the area and a number of proposals for reform.

## I. History of Regulation of Direct-to-Consumer Advertising

Pharmaceutical companies traditionally advertised only to physicians and other medical professionals.<sup>1</sup> This was because physicians used to be the sole decision-makers when it came to medical treatment.<sup>2</sup> Since the 1990s, these companies have increasingly advertised directly to consumers through newspaper, magazine, and television advertisements,<sup>3</sup> as patients became more involved in their healthcare decisions.<sup>4</sup> Companies choose to advertise directly to consumers for many reasons, such as to trigger them to visit their physicians for previously untreated conditions, to accelerate transitions to newer drugs by making consumers aware of such new pharmaceuticals, and to create and maintain brand loyalty.<sup>5</sup>

There are three types of drug advertisements targeted directly to consumers.<sup>6</sup> There are health-seeking advertisements which educate consumers about a certain disease or condition without mentioning a specific drug.<sup>7</sup> There are also reminder advertisements which name a drug but provide no information on use, efficacy, or risks.<sup>8</sup> These two types of advertisements do not need to meet most of the requirements of FDA regulations on advertisements, such as the brief summary and fair balance, because they do not discuss the efficacy of the drug.<sup>9</sup> The third category is the product-specific advertisement, which is the most common type of DTC advertisement.<sup>10</sup> These advertisements promote a certain drug, describe its use, and present

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<sup>1</sup> Lars Noah, *Advertising Prescription Drugs to Consumers: Assessing the Regulatory and Liability Issues*, 32 Ga. L. Rev. 141, 141 (1997).

<sup>2</sup> Francis B. Palumbo and C. Daniel Mullins, *The Development of Direct-to-Consumer Prescription Drug Advertising Regulation*, 57 Food & Drug L.J. 423, 424 (2002).

<sup>3</sup> Lars, *supra* note 1, at 141.

<sup>4</sup> Palumbo, *supra* note 2.

<sup>5</sup> Lars, *supra* note 1, at 150.

<sup>6</sup> Michael S. Wilkes et al., *Direct-to-Consumer Prescription Drug Advertising: Trends, Impacts, and Implications*, 19: 2 Health Affairs 110, 114 (2000).

<sup>7</sup> *Id.*

<sup>8</sup> *Id.*

<sup>9</sup> Palumbo, *supra* note 2, at 429.

<sup>10</sup> Wilkes et al, *supra* note 6.

information on safety and effectiveness.<sup>11</sup> The discussion in this paper addresses this third type of DTC advertisements.

The FDA has had authority over prescription drug promotional material since the passage of the Kefauver-Harris amendments in 1962.<sup>12</sup> The regulations promulgated at this time addressed promotions directed to medical professionals,<sup>13</sup> which was appropriate given the paternalistic nature of the doctor-patient relationship at this time.<sup>14</sup> In 1981, pharmaceutical companies proposed advertising directly to consumers, advocating increased public access to knowledge about drugs.<sup>15</sup> At this time, there was also a general trend in the political climate of increasing consumer sovereignty and empowering individuals with the ability to participate in their healthcare decisions.<sup>16</sup> The FDA requested a voluntary moratorium on such advertising to further analyze the issue.<sup>17</sup> In 1985, following the completion of several studies analyzing DTC advertising, the FDA lifted the moratorium.<sup>18</sup> The FDA requested that pharmaceutical manufacturers submit their DTC ads for preliminary comments.<sup>19</sup>

The FDA allowed for direct advertising, but only if the manufacturers abided by the existing regulations.<sup>20</sup> This included the “brief summary,” still seen in the current regulations, which required a true statement of information of side effects, contraindications, and

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<sup>11</sup> Wilkes et al, supra note 6.

<sup>12</sup> Palumbo., supra note 2, at 426. The 1962 amendments transferred regulatory authority over prescription drug advertising from the FTC to the FDA while authority over the advertising of over-the-counter drugs remained with the FTC. At this time, Congress was mostly concerned with advertising to medical professionals, and it is unlikely that there was the intent to have DTC advertising of prescription drugs under the FDA’s jurisdiction. *Id.* at 426-27.

<sup>13</sup> Lars, supra note 1, at 142.

<sup>14</sup> Wilkes et al., supra note 6, at 113.

<sup>15</sup> *Id.*

<sup>16</sup> *Id.*

<sup>17</sup> Lars, supra note 1, at 147-48.

<sup>18</sup> Michie Hunt, *Direct-to-Consumer Advertising of Prescription Drugs*, National Health Policy Forum, April 1998. Most of the studies concluded that consumers wanted more information on prescription drugs, and that consumers would tend to view such direct advertising as favorable. An FDA-commissioned study further concluded that risk and benefit information could both be conveyed through such direct advertising, in both print and broadcast form. *Id.* at 3.

<sup>19</sup> Wilkes et al., supra note 6, at 113.

<sup>20</sup> *Id.*

effectiveness of the advertised drug.<sup>21</sup> The industry argued that this requirement resulted in lengthy paper advertisements which consumers would not read, and that this practically prevented the use of broadcast advertisements.<sup>22</sup> In response, the FDA published the *Consumer-Directed Broadcast Advertisements* Guidance in 1997, which addressed requirements for DTC advertising to the industry.<sup>23</sup> For broadcast advertisements, only major side effects and contraindications must be presented as long as there is adequate provision for dissemination of labeling in connection with the presentation.<sup>24</sup> The adequate provision requirement can be met by providing a toll-free number, an Internet website, a recommendation to ask a physician or pharmacist for more information, and a reference to a print advertisement or brochures in a publicly accessible place.<sup>25</sup> The combination of more aggressive marketing by manufacturers and the FDA's acceptance of this type of advertising in hopes for a more educated patient population have led to the increased use of DTC advertising since the issuing of the Draft Guidance.<sup>26</sup>

Current regulations do not require FDA approval of advertisements prior to dissemination, except in certain situations.<sup>27</sup> Manufacturers may submit advertisements to the FDA prior to publication for comment.<sup>28</sup> The information in the advertisement must present a “fair balance” between information relating to side effects and contraindications and information relating to

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<sup>21</sup> 21 C.F.R. Section 202.1.

<sup>22</sup> Wilkes et al., supra note 6, at 113-14. *See, also*, Hunt, supra note 18, at 4 (Manufacturers often resorted to the other two types of advertisements, reminder and health-seeking ads, to avoid the strict regulations. However, this could also backfire. FDA ordered removal of an ad of a woman “windsurfing” through a wheat field because consumers could usually figure out that Allegra, the drug that the manufacturer was implicitly advertising, was used to treat allergies.).

<sup>23</sup> US Food and Drug Administration, *Patient and Physician Attitudes and Behaviors Associated With DTC Promotion of Prescription Drugs- Summary of FDA Survey Research Results* (2004).

<sup>24</sup> 21 C.F.R. Section 202.1.

<sup>25</sup> Division of Drug Marketing, Advertising, and Communications FDA, *Guidance for Industry: Consumer-Directed Broadcast Advertisements* (1997).

<sup>26</sup> Wilkes et al., supra note 6.

<sup>27</sup> 21 C.F.R. Section 202.1.

<sup>28</sup> *Id.*

effectiveness.<sup>29</sup> Advertisements that are false, lacking in fair balance, or otherwise misleading lead to a drug being misbranded.<sup>30</sup> This includes the use of any pictorial or graphic matter that is misleading in any way.<sup>31</sup> Due to the audiovisual nature of television commercials, advertisers may have an advertisement that does not violate the FDA regulations at first glance, but could be found to be misleading because of contradictory messages between the audio and visual components which minimize risk information compared to benefit information.<sup>32</sup> When the FDA identifies a violation, it sends a regulatory letter asking the manufacturer to cease dissemination of the advertisement.<sup>33</sup>

Proponents argue that direct-to-consumer advertising informs consumers of their choices and allows them to participate more meaningfully in their medical decisions.<sup>34</sup> The advertisements can make patients aware of underlying conditions, and can act as a springboard to a thorough medical examination with a physician.<sup>35</sup> Some studies have shown that patients report greater involvement in medical decisions and better compliance with their treatment regimens, suggesting there has been a positive impact of DTC advertising.<sup>36</sup> There are also suggestions that DTC advertising will decrease drug costs.<sup>37</sup> If there are competitors, advertising can reduce costs by promoting competition between different brands of drugs.<sup>38</sup>

Critics of direct-to-consumer advertising argue that these promotions play on consumer vanity or insecurity to increase demand, suggesting there will be more inappropriate use of

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<sup>29</sup> *Id.*

<sup>30</sup> *Id.*

<sup>31</sup> *Id.*

<sup>32</sup> Kelly N. Reeves, *Direct-to-Consumer Broadcast Advertising; Empowering the Consumer or Manipulating a Vulnerable Population?*, 53 Food & Drug L.J. 661, 674 (1998).

<sup>33</sup> Martin T. Gahart et al., *Examining The FDA's Oversight Of Direct-To-Consumer Advertising*, 3 Health Affairs 120 (2003).

<sup>34</sup> Lars, supra note 1, at 177-78.

<sup>35</sup> Wilkes et al, supra note 6, at 123.

<sup>36</sup> Balaji Datti and Mary W. Carter, *The Effect of Direct-to-Consumer Advertising on Prescription Drug Use by Older Adults*, 23:1 Drugs Aging 71, 72 (2006).

<sup>37</sup> FDA, supra note 23.

<sup>38</sup> Wilkes et al, supra note 6, at 122.

medical treatment.<sup>39</sup> A report by the United States General Accounting Office found that sales of drugs with the highest DTC spending have risen more quickly than the sales of other drugs.<sup>40</sup> The rise in sales was due to increased utilization rather than price increases, suggesting that DTC advertisements have led to increased use of prescription drugs.<sup>41</sup>

Critics also predict that DTC advertising will increase costs of treatment.<sup>42</sup> Although advertising may reduce prices in other industries, this is unlikely to occur with prescription drugs because prices are not usually presented in a DTC advertisement and higher prices may not reduce demand because consumers often have health insurance plans which pay for their medications.<sup>43</sup> Furthermore, DTC advertising is often used for driving sales of newer, more expensive products for symptomatic relief of chronic conditions, which carry huge market potential.<sup>44</sup> These drugs are often still covered by patent protection, and therefore can retain premium prices.<sup>45</sup> High prices combined with greater utilization rates can lead to a massive increase in total healthcare costs.

There is also an inherent conflict between the goal of empowering consumers in their medical decisions and the promotional interests of the pharmaceutical industry, as a desire for increased sales for a particular drug may align with rational prescribing of treatments for patients.<sup>46</sup> It may be contradictory to require that these drugs be prescribed through a medical professional who has expert knowledge, yet allow marketing to consumers who lack that

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<sup>39</sup> Lars, *supra* note 1, at 169-70.

<sup>40</sup> United States General Accounting Office, *Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising Has Limitations*, GAO-03-177 (2002).

<sup>41</sup> *Id.*

<sup>42</sup> FDA, *supra* note 23.

<sup>43</sup> Wilkes et al, *supra* note 6, at 122.

<sup>44</sup> Matthew F. Hollon, *Direct-to-Consumer Advertising: A Haphazard Approach to Health Promotion*, 293 JAMA 2030, 2030 (2005). *See, also*, USGAO, *supra* note 40 (All of the top 15 DTC-advertised drugs in 2000 were for chronic conditions, such as allergy/asthma, high cholesterol, and arthritis, and all but 1 of the top 50 drugs were for non-episodic conditions).

<sup>45</sup> USGAO, *supra* note 40.

<sup>46</sup> Wilkes et al, *supra* note 6, at 113.



expertise.<sup>47</sup> Furthermore, the optimal treatment for a medical condition often includes non-medical interventions such as stress management or diet and exercise.<sup>48</sup> A DTC advertisement stressing the use of a particular drug for that condition could interfere with the patient's willingness to accept a physician's comprehensive treatment plan.<sup>49</sup>

There is also serious doubt as to whether DTC advertisements really can educate about a particular condition.<sup>50</sup> One study of existing advertisements found that although most advertisements gave the name of a drug and symptoms of a condition, few identified a cause or risk factor of the condition, described prevalence information, or clarified any misconceptions.<sup>51</sup> The majority of advertisements did not acknowledge any other alternative therapies, medical or non-medical.<sup>52</sup> If the educational quality of these advertisements is highly variable, this weakens one of the primary arguments of DTC proponents.

In 2004, FDA published results from two patient surveys and one physician survey which analyzed the effects of DTC advertising on healthcare, from both a public health and doctor-patient perspective.<sup>53</sup> Although DTC advertising seemed to increase patient awareness of health and treatment, there was no evidence of increased visits as a result of this advertising.<sup>54</sup> The report suggests that the usefulness of the "brief summary" is hampered by the technicality of the language, and proposes that the information should be presented in more consumer friendly formats and language.<sup>55</sup> About half of the physicians surveyed reported feeling at least a little pressure to prescribe specific drugs when requested by their patient who had seen a DTC

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<sup>47</sup> *Id.* at 116.

<sup>48</sup> *Id.* at 121.

<sup>49</sup> *Id.*

<sup>50</sup> *Id.* at 116.

<sup>51</sup> Dominick L, Frosch et al., *Creating Demand for Prescription Drugs: A Content Analysis of Television Direct-to-Consumer Advertising*, 5 *Annals of Family Medicine* 1 (2007).

<sup>52</sup> *Id.*

<sup>53</sup> FDA, *supra* note 23.

<sup>54</sup> *Id.*

<sup>55</sup> *Id.*

advertisement.<sup>56</sup> Both patients and physicians thought that DTC advertisements overstated drug efficacy and did not present a fair balance of benefits and risks of drugs, and fewer patients in the 2002 survey, compared to the 1999 survey, indicated that DTC advertisements were helpful in their interactions with their physicians.<sup>57</sup> Although the results suggest that while patients believe they are skeptical of DTC advertisements, physicians believe that their patients are still being misled or confused by them.<sup>58</sup> Ultimately, the report concluded that there were both positive and negative effects of DTC advertising on public health and the doctor-patient interaction, and invited further research on the topic without issuing an opinion on whether regulation in the area should be tightened or loosened.<sup>59</sup>

There has been much criticism on the FDA's actions concerning DTC advertising.<sup>60</sup> Despite increased use of resources by manufacturers on DTC advertising, the number of regulatory actions fell dramatically during the period from 1997 to 2006.<sup>61</sup> This was likely a result of weakened FDA capacity to enforce advertising regulations.<sup>62</sup> For example, although spending on DTC advertisements increased by 45% between 2002 and 2004, the number of FDA staff members reviewing these advertisements only increased from three to four in the same period.<sup>63</sup> Furthermore, the proportion of broadcast advertisements that were approved by FDA prior to airing declined from 64% in 1999 to 32% in 2004.<sup>64</sup> Manufacturers who voluntarily

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<sup>56</sup> *Id.*

<sup>57</sup> *Id.*

<sup>58</sup> *Id.*

<sup>59</sup> *Id.*

<sup>60</sup> Julie M. Donahue et al., *A Decade of Direct-to-Consumer Advertising of Prescription Drugs*, 357 N. Engl. J. Med. 673, 674 (2007).

<sup>61</sup> *Id.* at 679.

<sup>62</sup> *Id.*

<sup>63</sup> *Id.*

<sup>64</sup> *Id.*

submit their advertisements for pre-dissemination approval could face delayed review, which discourages them from submission.<sup>65</sup>

The speed of enforcement action has also greatly declined.<sup>66</sup> A regulation issued in 2002 requires that the FDA's Office of Chief Counsel review and approve all regulatory letters.<sup>67</sup> Prior to this regulation, FDA officials reported that regulatory letters were issued within several days of the receipt of a misleading advertisement.<sup>68</sup> In contrast, the OCC's goal in reviewing draft regulatory letters is within 45 working days, which does not include any time that the Department of Health and Human Services takes to revise the letter at the order of the OCC.<sup>69</sup>

This delay in enforcement action can lead to misleading advertisements completing their broadcast life cycle before such regulatory letters are even issued.<sup>70</sup> One-fifth of DTC advertisements air for only a month, and one-third air for two months or less.<sup>71</sup> For five draft letters submitted by the DDMAC between January and September of 2002, the number of days between submission and issuance ranged from 13 to 78 calendar days.<sup>72</sup> Although it is unknown whether DTC advertisements for those specific drugs had a short airing period, it is clearly possible for regulatory letters to reach manufacturers after their misleading advertisements had been aired for a significant period of time.<sup>73</sup>

The breadth and timing of FDA review may also lead to problems. The FDA targets its reviews to the advertisements that receive the greatest exposure,<sup>74</sup> which may lead to less-

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<sup>65</sup> *Id.* at 679-80.

<sup>66</sup> USGAO, *supra* note 40.

<sup>67</sup> *Id.*

<sup>68</sup> *Id.*

<sup>69</sup> *Id.* The HHS has responded that the purpose of requiring OCC approval was to ensure that regulatory letters had a solid legal foundation in order to promote compliance. However, FDA regulatory letters issued prior to this regulatory had already been successful in ceasing dissemination of the identified misleading advertisements. *Id.*

<sup>70</sup> *Id.*

<sup>71</sup> *Id.*

<sup>72</sup> *Id.* The five letters were issued 13, 22, 39, 55, and 78 days after submission. *Id.*

<sup>73</sup> *Id.*

<sup>74</sup> *Id.*

disseminated advertisements falling through the cracks. Furthermore, since companies submit advertisements for comments when they begin dissemination, the FDA cannot prevent misleading advertisements from reaching the public. Even if the FDA could adequately review all of the submitted advertisements, it is limited in its ability to police advertisements which were not submitted.<sup>75</sup> As of the USGAO report in 2002, the FDA contracted with a commercial service to monitor pharmaceutical advertisements that were broadcast on television.<sup>76</sup> The service, however, only monitored the six major cable television networks, the New York City affiliates of the four major networks, and PBS.<sup>77</sup> This could miss smaller cable television networks and local markets, which could lead to misleading advertisements remaining for long periods of time in certain locations.<sup>78</sup>

There is also no requirement that a drug be on the market for a certain amount of time before DTC advertising can commence. DTC advertisements often start after a drug has been on the market for only a year, so there is potential of wide dissemination of drugs with unknown long-term safety profiles.<sup>79</sup>

Another criticism of FDA enforcement is the lack of use of harsher remedies, such as seizing drugs for which there have been misleading advertisements or directing a company to run corrective campaigns.<sup>80</sup> Although FDA officials have stated that they have not resorted to such measures because companies have generally complied with their regulatory letters and the FDA does not want to remove beneficial drugs from the market, there have been repeat offenders who have received multiple regulatory letters for different advertisements promoting the same drug.<sup>81</sup>

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<sup>75</sup> *Id.*

<sup>76</sup> *Id.*

<sup>77</sup> *Id.*

<sup>78</sup> *Id.* As an example, a misleading advertising was broadcast in Puerto Rico for 2 years. *Id.*

<sup>79</sup> Donahue et al, supra note 60 at 678-79.

<sup>80</sup> Gahart et al, supra note 33, at 121.

<sup>81</sup> *Id.* at 122.

This suggests that FDA enforcement is not providing adequate deterrence, even for those companies who have actually been the target of enforcement actions.<sup>82</sup>

DTC advertising continues to be a controversial subject, especially with what some feel is a lack of policing by the FDA.

## II. DTC Advertising and Alzheimer's Disease

Alzheimer's disease is the most common cause of dementia, affecting one out of eight Americans over the age of 65, and leads to debilitation of cognitive and motor function and, eventually, death.<sup>83</sup> It is the sixth leading cause of death and has a slow, insidious progression with survival after diagnosis averaging four to eight years, but ranging up to twenty years.<sup>84</sup> Secondary diseases such as depression and anxiety also often result upon diagnosis.<sup>85</sup> Symptoms commonly begin with mild cognitive impairment, such as patchy memory loss and subtle behavioral changes.<sup>86</sup> This progresses to moderate impairment with agitation and combativeness, and possible delusions and hallucinations.<sup>87</sup> Severe impairment is characterized by inability to speak or comprehend language and complete dependence on others to complete basic life functions.<sup>88</sup>

With the exception of certain rare, inherited forms of the disease, the exact physiologic changes in the brain that lead to Alzheimer's remain unknown.<sup>89</sup> Diagnosis is made by the

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<sup>82</sup> *Id.* For example, the FDA issued four letters to Glaxo Wallcome for its advertising of the allergy drug Flonase in 1999 and 2000, and four letters to Pfizer in a span of four years for its advertising of Lipitor. *Id.*

<sup>83</sup> Alzheimer's Association. *2012 Alzheimer's disease facts and figures*, 8 *Alzheimer's and Dementia: The Journal of the Alzheimer's Association* 131 (2012).

<sup>84</sup> *Id.*

<sup>85</sup> Anna A. Theodorou et al., *Drug Utilization Patterns in Patients With Alzheimer's Disease*, 2 *The American Journal of Pharmacy Benefits* 77 (2010).

<sup>86</sup> Philip D. Sloane et al., *The Public Health Impact of Alzheimer's Disease, 2000-2050: Potential Implication of Treatment Advances*, 23 *Annu. Rev. Public Health* 213, 213 (2002).

<sup>87</sup> Theodorou et al., *supra* note 85, at 80.

<sup>88</sup> Sloane et al, *supra* note 86 at 213; Theodorou et al., *supra* note 85, at 80.

<sup>89</sup> Alzheimer's Association, *supra* note 83.

physician through a combination of medical and family history and various cognitive tests and neurologic examinations,<sup>90</sup> but there is no definitive diagnostic test.<sup>91</sup> Input from a family member or another individual close to the patient can be very important in tracing cognitive and behavioral changes.<sup>92</sup> Although the cause or causes of Alzheimer's disease are not yet known, there is general agreement that there are multiple factors involved, with interaction between genes and the environment.<sup>93</sup> Connections have also been suggested between lifestyle and Alzheimer's disease.<sup>94</sup>

There are currently only five FDA-approved drugs and these drugs only treat the symptoms of the disease.<sup>95</sup> Drug efficacy is often short-lived, usually lasting from a few months to a few years.<sup>96</sup> However, active medical management can significantly improve quality of life for patients and their caregivers.<sup>97</sup> There is also ongoing research on alternative methods of treatment, such as music therapy.<sup>98</sup>

The FDA-approved drugs fall into two categories: acetylcholinesterase inhibitors and NMDA receptor antagonists.<sup>99</sup> The four approved cholinergic drugs, Donepezil, Rivastigmine,

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<sup>90</sup> *Id.*

<sup>91</sup> Sloane et al., *supra* note 86, at 215.

<sup>92</sup> Alzheimer's Association, *supra* note 83.

<sup>93</sup> Mark P. Mattson, *Pathways Towards and Away from Alzheimer's Disease*, 430 *Nature* 631, 631-33 (2004). Alzheimer's disease is characterized by destruction of neurons and degeneration of synapses between neurons. Definitive diagnosis requires postmortem examination of the brain and the presence of "plaques" and "tangles." These are mainly found in the brain regions involved in memory and emotion. Cellular abnormalities result in the formation of these plaques and tangles, and many genes involved in these cellular abnormalities may be linked to susceptibility to Alzheimer's disease. Other risk factors may be a low education level and history of head trauma *Id.*

<sup>94</sup> *Id.* at 633. Epidemiological studies have associated high-calorie and high-fat diets and a sedentary lifestyle with an increased risk of Alzheimer's disease. A link with high cholesterol levels has also been suggested. Exercise may also provide neuroprotective effects. *Id.*

<sup>95</sup> Alzheimer's Association, *supra* note 83.

<sup>96</sup> Theodorou et al., *supra* note\_ at 78.

<sup>97</sup> Alzheimer's Association, *supra* note 83.

<sup>98</sup> Javier Olazarán et al., *Nonpharmacological Therapies in Alzheimer's Disease: A Systematic Review of Efficacy*, 30 *Dement Geriatr Cogn Disord* 161 (2010). Other nonpharmacological therapies include cognitive training, reminiscence, light therapy, and muscle relaxation. Therapies for caregivers include education, support, and respite care. *Id.*

<sup>99</sup> Francesca Mangialasche, et al., *Alzheimer's Disease: Clinical Trials and Drug Development*, 9 *Lancet Neurol* 702, 703 (2010).

Galantamine, and Tacrine,<sup>100</sup> most likely work by mitigating the decrease in the neurotransmitter acetylcholine in the brains of Alzheimer's disease patients.<sup>101</sup> These drugs can improve cognition, behavior, and functional and global clinical state.<sup>102</sup> However, since they can only maintain neurotransmitter levels, and cannot prevent destruction of the neurons producing neurotransmitters, their effectiveness may drop as the disease progresses.<sup>103</sup> Galantamine and Rivastigmine are approved for treating symptoms in mild to moderate Alzheimer's disease, while Donepezil is approved for all stages.<sup>104</sup> Memantine is the only approved non-cholinergic drug.<sup>105</sup> It works through a completely different mechanism: regulating levels of glutamate, another neurotransmitter.<sup>106</sup> Memantine can reduce clinical deterioration in moderate-to-severe Alzheimer's disease.<sup>107</sup> Since the cholinergic drugs and Memantine work through different mechanisms, both a cholinergic drug and Memantine can be prescribed together.<sup>108</sup> Other pharmacological strategies include the use of nonsteroidal agents such as aspirin or ibuprofen to

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<sup>100</sup> NIH Publication No. 08-3431, *Alzheimer's Disease Medications Fact Sheet*, (2008, updated 2010), available at <http://www.nia.nih.gov/sites/default/files/ADMedsFS.pdf>. Tacrine is rarely prescribed now because of safety concerns. *Id.*

<sup>101</sup> Mangialasche, supra note 99, at 702. One characteristic of Alzheimer's diseases is the early loss of basal forebrain cholinergic neurons, which normally produce the neurotransmitter acetylcholine. Acetylcholinesterase is an enzyme which breaks down acetylcholine released by neurons. The cholinergic drugs function by inhibiting acetylcholinesterase, which results in slower breakdown of acetylcholine, which thus helps mitigate the decreased release of acetylcholine. *Id.*

<sup>102</sup> *Id.* at 703.

<sup>103</sup> NIH Fact Sheet, supra note 100.

<sup>104</sup> *Id.*

<sup>105</sup> Mangialasche, supra note 99 at 702.

<sup>106</sup> Jon W Johnson and Shawn E Kotermanski, *Mechanism of action of memantine*, 6 Current Opinion in Pharmacology 61 (2006). Alzheimer's disease is also characterized by deficits in glutamatergic neurotransmission. There have been several explanations for the cognitive benefits of Memantine, including reducing noise from excessive neurotransmitter receptor activation, inhibition of beta-amyloid toxicity, and readjustment of the balance between inhibition and activation of neurons. *Id.*

<sup>107</sup> Barry Reisberg et al., *Memantine in Moderate-to-Severe Alzheimer's Disease*, 348 N. Engl. J. Med. 1333 (2003). The study reported greater tolerability of Memantine compared to the gastrointestinal side effect profile of cholinergic drugs, and emphasized alleviation of symptoms in patients with moderate-to-severe Alzheimer's disease, with a lower average Mini-Mental State Examination base line score than that used in the donepezil study on moderate-to-severe Alzheimer's disease. *Id.*

<sup>108</sup> NIH Fact Sheet, supra note 100.

reduce inflammatory responses, enhancing putative protective factors through supplements such as vitamin E, and treating concomitant cardiovascular risk factors, such as hypertension.<sup>109</sup>

Research on Alzheimer's disease has not come up with any disease-modifying drugs yet, although there are many ongoing clinical and experimental studies.<sup>110</sup> Developing effective drugs is especially difficult because of the complexity of the disease and lack of knowledge about its causes and mechanism of action.<sup>111</sup> There are likely several levels of interaction (between genes, proteins, cells, etc.) and multi-targeted therapies may be the most effective.<sup>112</sup>

The impact of Alzheimer's disease extends beyond the patient. Over fifteen million Americans provide unpaid care for an individual with dementia, mostly for family members.<sup>113</sup> The sum of reimbursable, non-reimbursable, and unpaid labor costs in caring for an elderly patient at home may be as expensive as nursing home care.<sup>114</sup> Many of these caregivers report high levels of emotional stress and depression from providing care to their loved ones.<sup>115</sup> Research also shows that this stress can lead to deterioration in physical health, including development of metabolic syndrome and increased risk of cardiovascular diseases.<sup>116</sup> Treatments for Alzheimer's disease can therefore significantly reduce costs not only for patients but also for their families.

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<sup>109</sup> Sloane et al, supra note 86, at 217.

<sup>110</sup> Mangialasche, supra note 99 at 712.

<sup>111</sup> *Id.*

<sup>112</sup> *Id.* Multi-target therapies could involve prescription of several individual drugs, combinations of active ingredients in one drug, or designing of a single compound that has effects on multiple Alzheimer's disease-related mechanisms. *Id.*

<sup>113</sup> Alzheimer's Association, supra note 83.

<sup>114</sup> Jennifer J. Dunkin and Cay Anderson-Hanley, *Dementia Caregiver Burden: A Review of the Literature and Guidelines for Assessment and Intervention*, 51 *Neurology* 53 (1998).

<sup>115</sup> Alzheimer's Association, supra note 83. *See, also*, Leah D. Clyburn et al., *Predicting Caregiver Burden and Depression in Alzheimer's Disease*, 55B *Journal of Gerontology* S2 (2000) (Many studies have found caregivers are at a greatly increased risk of depression).

<sup>116</sup> Alzheimer's Association, supra note 83.



The global burden of Alzheimer's disease is expected to increase dramatically in the next few decades as the world population ages.<sup>117</sup> One model predicts that the prevalence of the disease will quadruple from 26.6 million persons affected worldwide in 2006 to 106.2 million by 2050.<sup>118</sup> Another study predicted that without any major therapeutic advances, 10.2 million persons will have the disease in the U.S. in 2050.<sup>119</sup> In 1995, a mid-range estimate of the total cost of Alzheimer's disease care was \$38,000 per patient per year, or \$65 billion nationally.<sup>120</sup> This will increase proportionately to the increased prevalence by 2050. The significance of any breakthrough in treatment is shown by an estimate that a six-month delay in disease onset would save approximately \$18 billion annually after fifty years.<sup>121</sup>

Alzheimer's disease is an issue of significance for the FDA. In 2007, the Commissioner of the FDA made a statement about the FDA's role in development of treatment for Alzheimer's disease in front of a Senate subcommittee on Retirement Security and Aging.<sup>122</sup> With the increasing prevalence of the disease and the aging population, the FDA recognized Alzheimer's as a disease that may cause great burdens on the American health system in the future.<sup>123</sup> Despite advancements in research on potential causes of the disease, many researchers emphasize the complexity of the disease and the necessity of approaching treatment possibilities from multiple directions.<sup>124</sup> The FDA is currently engaged in many projects that involve research and treatment of Alzheimer's disease. This includes the Patient Representative Program, which will provide

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<sup>117</sup> Ron Brookmeyer et al., *Forecasting the Global Burden of Alzheimer's Disease*, 3 *Alzheimer's & Dementia* 186 (2007).

<sup>118</sup> *Id.* at 190.

<sup>119</sup> Sloane et al., *supra* note 86, at 224.

<sup>120</sup> *Id.* at 217.

<sup>121</sup> *Id.*

<sup>122</sup> Statement of Andrew C. von Eschenbach, 2007, available at <http://www.fda.gov/NewsEvents/Testimony/ucm110879.htm>

<sup>123</sup> *Id.*

<sup>124</sup> *Id.*

patient and caregiver insight into regulations on the disease.<sup>125</sup> Specifically, to address the problem of diminishing intellectual function of patients with the disease, the FDA has agreed to include patient and caregiver couples in the program so that caregiver insight can continue even after the patient can no longer participate due to the debilitating nature of the disease.<sup>126</sup> Furthermore, the FDA has a Neurology Working Group and is engaged in a study with the NIH in acquiring information about Alzheimer's.<sup>127</sup> The FDA is therefore heavily involved in research on Alzheimer's disease and the potential impact of the disease on the American public. The influence of DTC advertising on Alzheimer's disease patients and their families should be an issue of interest for the FDA given their involvement in researching the disease and its treatment.

There are many reasons that drug manufacturers advertise Alzheimer's drugs directly to consumers. DTC advertisers are likely to develop drugs that have only been marginally treatable or untreatable until recently, like Alzheimer's disease.<sup>128</sup> These drugs often can be sold at premium prices because of patent protection.<sup>129</sup> Furthermore, given that the majority of ads promote drugs that maintain chronic conditions, Alzheimer's is a lucrative target because of its prolonged progression and incurability.<sup>130</sup> The policy issues that address such "breakthrough" drugs are especially difficult because these drugs are often medically warranted and lack therapeutic alternatives.<sup>131</sup> Manufacturers may be able to charge a higher price and consumers may demand the drug once they are informed about it through advertising.<sup>132</sup> Although the drug may be beneficial, there is the societal cost from the pressure exerted on physicians and insurers

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<sup>125</sup> *Id.*

<sup>126</sup> *Id.*

<sup>127</sup> *Id.*

<sup>128</sup> Hunt, *supra* note 18.

<sup>129</sup> *Id.* at 12.

<sup>130</sup> *Id.* at 12.

<sup>131</sup> Hunt, *supra* note 18, at 13.

<sup>132</sup> *Id.*

from dissemination of knowledge of the drug by DTC advertising.<sup>133</sup> These problems are likely to be especially pronounced for treatments of Alzheimer's disease given the relatively low number of available drugs.

Advertising for Alzheimer's disease drugs, as for many other prescription drugs, is targeted towards older adults in the American population. Given the tremendous costs of healthcare and the projected prevalence of Alzheimer's disease, any effect on healthcare as a result of DTC advertising could significantly affect medical costs in the U.S. A relatively recent study by Datti et al. on the effect of DTC advertising on older adults suggests a significant impact, although it is difficult to tell whether the increased costs are outweighed by the benefits.<sup>134</sup> The study found that although older adults are less likely than younger adults to request a specific drug following DTC advertising, older adults are more likely to be referred for additional medical services.<sup>135</sup> The study could not answer whether this increased referral rate was beneficial in that conditions could be diagnosed earlier or more effective therapy could be offered, or if it was harmful by encouraging expensive and unnecessary treatments.<sup>136</sup> The article also notes how new Medicare provisions that offer better compensation for medications for older adults could make patients more likely to request DTC drugs and therefore amplify the results in their study.<sup>137</sup> All of these results suggest that increased DTC advertising for Alzheimer's disease has the potential of increasing use of healthcare services.

Older adults are also more likely than their younger counterparts to believe they are not as affected by DTC advertising as others.<sup>138</sup> One study found that in general, consumers believe

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<sup>133</sup> *Id.* at 13-14.

<sup>134</sup> Datti et al., *supra* note 36 at 78.

<sup>135</sup> *Id.*

<sup>136</sup> *Id.*

<sup>137</sup> *Id.*

<sup>138</sup> Denise E. Delorme et al., "*Others Are Influence, But Not Me*": Older adults' perceptions of DTC prescription drug advertising effects, 21 *Journal of Aging Studies* 135 (2006).

DTC ads exert more influence on others than on themselves, and that this third-person effect was magnified for negative ad effects compared to positive effects.<sup>139</sup> A further study by the same group found that older adults may underestimate the effects on DTC advertising on themselves.<sup>140</sup> While the surveyed adults denied DTC ad effects on themselves, their answers on other questions showed that they exhibited DTC-ad-expected behaviors such as learning about drug benefits and risks, talking with friends and relatives, and searching for more information by talking to a doctor or using the Internet.<sup>141</sup> Influences of DTC advertising, including those for Alzheimer's disease, are therefore likely to have more of a hidden impact on older adults than younger adults due to this misperception.

Another source of concern for DTC advertising for Alzheimer's disease is the alternative target of marketing. As previously mentioned, the emotional and physical impact on caregivers of Alzheimer's disease patients can itself result in a burden on public health. One study found that advertisements for the Alzheimer's disease drug Aricept frequently appeared in magazines read most commonly by women in their forties.<sup>142</sup> Advertising of treatments for Alzheimer's appeals not only to the patient suffering from the disease but also to the caregiver who is looking to improve the quality of life of his or her loved one, which indirectly improves the caregiver's quality of life as well. Although there is the potential of saved costs from both of these classes of individuals, there is also added vulnerability as caregivers are looking for any source of help for the patient. Since these drugs can only address the symptoms of Alzheimer's disease and may not help an individual patient at all, the added stress from failed treatment for both the patient and caregiver could add to the costs of increased DTC advertising.

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<sup>139</sup> Huh, et al., *The Third-Person Effect and Its Influence on Behavioral Outcomes in a Product-Advertising Context: The Case of Direct-to-Consumer Prescription Drug Advertising*, 31 *Communication Research* 568 (2004).

<sup>140</sup> Delorme et al., *supra* note 138 at 147.

<sup>141</sup> *Id.*

<sup>142</sup> Steven Woloshin et al., *Direct-to-Consumer Advertisements for Prescription Drugs: What Are Americans Being Sold?*, 358 *The Lancet* 1141, 1145 (2001).

The Datti article notes how DTC advertising targeted to individuals other than the patients could affect the results of their study.<sup>143</sup> Since older Alzheimer’s disease patients are targeted from multiple directions through DTC advertising, the results from the Datti study may be underestimated.<sup>144</sup> The Datti study only asked whether older adults requested specific drugs for their own care after personally being exposed to a DTC advertisement.<sup>145</sup> This excludes situations where another adult who accompanied the patient requested a drug, or a patient requested a drug at the suggestion of a family member who was exposed to a DTC advertisement. These situations may have also led to referrals or extra treatments. This means that the potential effects on healthcare costs from DTC advertisement could be much higher than what is predicted from the results in the Datti study, which is another reason for the urgency and importance of analyzing this issue in more detail.

### **III. A Case Study: Aricept**

Aricept is the brand name for Donepezil, a cholinergic drug.<sup>146</sup> Aricept was approved by the FDA in 1996 and is manufactured by Eisai.<sup>147</sup> It is indicated for treatment of mild, moderate, and severe stages of Alzheimer’s disease.<sup>148</sup> This paper will analyze how Aricept is presented in its physician label, patient insert, and DTC television advertisements.

The Aricept Physician Prescribing Information starts off with a “Highlights” section and then has the longer detailed prescribing information section.<sup>149</sup> The full prescribing information

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<sup>143</sup> Datti, *supra* note 36.

<sup>144</sup> *Id.* at 80.

<sup>145</sup> *Id.* at 73-74.

<sup>146</sup> Aricept Label, available at

[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/020690s035,021720s008,022568s0051bl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020690s035,021720s008,022568s0051bl.pdf)

<sup>147</sup> Orange Book Detail Record Search for Aricept, Food & Drug Admin., available at

[http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl\\_No=020690&TABLE1=OB\\_Rx](http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=020690&TABLE1=OB_Rx).

<sup>148</sup> Aricept Label, *supra* note 146.

<sup>149</sup> *Id.*

contains information on the dosage and administration of the drug, contraindications, warnings, adverse reactions, pharmacology and toxicology, and description of the clinical studies that showed efficacy of the drug.<sup>150</sup> For adverse reactions, the label includes tables of the rates of adverse events during the clinical trials for different dosages and comparisons between placebo and drug, along with written summaries of the results.<sup>151</sup> The effectiveness of Aricept is described both graphically and verbally in the Clinical Studies section, which summarizes the results from various studies using different doses of the drug and for different stages of the disease.<sup>152</sup>

The Patient Insert for Aricept includes similar information, but in easier language and in much shorter form. Most of the insert discusses complications of the drug and instructions on how to take it, rather than the benefits.<sup>153</sup> There is only one section on benefits and it uses careful language so as to not overstate its claims.<sup>154</sup> It says that the drug “can help” with mental function and daily tasks, and that it does not work the same in all people.<sup>155</sup> It gives four possibilities of the effects of the drug: patient gets “much better,” patient gets better in “small ways” or stays the same, patient gets worse at a slower pace, and patient gets worse as expected.<sup>156</sup> The insert states that the drug does not cure Alzheimer’s disease and that all patients with the disease get worse over time, even if they take Aricept.<sup>157</sup> The rest of the insert is devoted to general information, ingredients, instructions, and some of the negative effects of taking the drug.<sup>158</sup> The major contraindication is allergic reaction, and the insert lists health problems to discuss with a

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<sup>150</sup> *Id.*

<sup>151</sup> *Id.*

<sup>152</sup> *Id.*

<sup>153</sup> *Id.*

<sup>154</sup> *Id.*

<sup>155</sup> *Id.*

<sup>156</sup> *Id.*

<sup>157</sup> *Id.*

<sup>158</sup> *Id.*

physician before taking Aricept.<sup>159</sup> There is also a list of serious side effects, followed by a list of the most common side effects.<sup>160</sup> The insert seems to be a fair assessment of the risks involved with taking the drug without an overstatement of the benefits. The listing of the four categories of effects of the drug makes it clear that the drug can improve symptoms, but also that it may just slow down progression of the disease.

The major difference between the physician label and the patient insert is the discussion of efficacy of the drug. While the patient insert simply lists four possible effects of the drug, the physician label introduces the results of the clinical studies. There is no information in the patient insert on the breakdown of which end result is more probable. There is also no information on symptoms of Alzheimer's disease. This highlights the importance of a thorough medical examination by a physician in deciding whether a patient is a candidate for use of a drug and explanation to the patient of the probability of improvement or slowing down of progression of a disease, regardless of whether the patient came to the doctor because of exposure to DTC advertising.

Two television advertisements for the drug have a clearly different approach and presentation of Aricept.<sup>161</sup> Both commercials are 60 seconds long and follow a similar structure. They start off with a person other than the patient talking to the viewer about when they became concerned about a loved one. One commercial is of a woman talking about her husband, and how he could not remember his granddaughter's name when they picked her family up at an airport one day (this ad will be referred to as "Airport" from now on). The other commercial is, again, of a woman, but this time talking about how her mother forgot that her daughter's family visits her

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<sup>159</sup> *Id.*

<sup>160</sup> *Id.*

<sup>161</sup> Aricept commercials, available at <https://adpharm.net/blog/2008/09/aricept-tv-commercial/>; [http://www.youtube.com/watch?v=6LeDE9Zpbnc&feature=results\\_video&playnext=1&list=PLAD55B2254404C927](http://www.youtube.com/watch?v=6LeDE9Zpbnc&feature=results_video&playnext=1&list=PLAD55B2254404C927)

every week on Sunday (this will be referred to as “Sunday”). This anecdote-type opening continues for about 15 seconds, with images of the confused-looking patient.

Both commercials then turn to the speaker and the patient visiting a doctor together, where they hear about Aricept being the only drug that is available for all stages of Alzheimer’s disease. There is also a scene of a doctor showing the patient and family member an image of two nerve cells and small bubbles traveling from one nerve cell to the other. Some of the bubbles are popping, while others form a dark rim around them. The commercial then goes on to explain the benefits of Aricept, and how it can slow symptoms of Alzheimer’s disease and can improve cognition. A little after the 30 second mark, both commercials go into the warnings and potential side effects of Aricept. While the narrator (a voice different from the original speaker) describes these risks of the drug, the visual image is a scene of the patient enjoying time with his or her family and responding to family members. This is presumably after the patient has taken the drug. In the “Airport” ad, the patient is seen on a family excursion and later picking photos for an album, and the viewer can hear the patient point to one picture and say he likes that one. In the “Sunday” ad, the patient is seen making a bed and helping set a table for dinner with the family. In the last five seconds, the message to go see a doctor is reiterated along with the slogan “don’t wait, Alzheimer’s isn’t waiting.”

Using the analysis structure of the Frosch article on DTC television advertising,<sup>162</sup> the commercials have the common story structure of using “before and after” images of a patient. Both make factual claims about symptoms. However, neither really goes into the biological nature or mechanism of the disease. Although the seemingly scientific image of the two nerve cells is shown, there is no explanation as to what the bubbles in between the nerve cells are and

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<sup>162</sup> Frosch, *supra* note 51, at 6.



what, if any, effect the drug is having on either the nerve cells or the bubbles in between.<sup>163</sup>

There is nothing labeled in the picture besides “nerve cells.” There is no information on risk factors, prevalence, or subpopulations at risk of the condition.

The appeals in the commercial are mostly positive and negative emotional appeals. Although there is some information about how the drug can improve function, they are done through the voice of the patient’s family member, which can be seen as more of a positive emotional appeal to the caregiver of a patient with Alzheimer’s disease. The lifestyle portrayals consist of showing how the disease interferes with the patient’s relations with family members and how the drug can improve the patient’s condition. There is no statement about alternative therapies to help with the condition. Finally, the commercials imply that Aricept is a medical breakthrough in that it is the only drug approved for all stages of Alzheimer’s disease.

These advertisements follow the pattern of the majority of such DTC advertisements that were studied in the Frosch article.<sup>164</sup> For example, both Aricept ads and the majority of the ads in the Frosch article provided some factual information about the disease, such as symptoms, but neglected to provide information on risk factors or prevalence.<sup>165</sup> Furthermore, the advertisements almost always used positive emotional appeal and some negative emotional appeal.<sup>166</sup> Another similarity is the reference to the drug being a medical breakthrough of some sort (being the only product that treats all stages of Alzheimer’s disease), which was seen in 58% of the advertisements in the Frosch study.<sup>167</sup>

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<sup>163</sup> With some background on the mechanism of cholinergic drugs, it can be inferred that the bubbles traveling between the nerve cells represent the neurotransmitter acetylcholine, and the drug is preventing the bubbles from popping, represented by the dark rim which is formed around some of them.

<sup>164</sup> Frosch, *supra* note 51, at 6.

<sup>165</sup> *Id.* at 9.

<sup>166</sup> *Id.*

<sup>167</sup> *Id.* at 10.

Given the similarity of the Aricept advertisements to those studied in the Frosch article, similar conclusions can be made about their potential impacts on viewers. First of all, the risk factors and symptoms of the disease are ambiguously defined, which can cause a large range of viewers to believe that treatment is necessary, even when they or their loved one does not have Alzheimer's.<sup>168</sup> The limited information on the disease may be contributing to increased medicalization of the American population.<sup>169</sup> For example, decreased cognition could be a sign of Alzheimer's, any other form of dementia, or just normal aging. The lack of clear information on what symptoms should be treated with Aricept will lead to a larger population of people believing that Aricept could be the solution to their problems than appropriate.

Furthermore, the use of positive and negative emotional appeals may cause viewers to discount factual information about risks and benefits and to seek treatment for clinically inappropriate reasons such as fear from not using the product or expectations of happiness if they do use the product.<sup>170</sup> This problem is likely to be accentuated in the case of Alzheimer's, because the commercial is directed to family members of patients as well as patients themselves. This is highlighted by the fact that the speakers of the two Aricept commercials are not the patients, but the patient's wife in the "Airport" ad and the patient's daughter in the "Sunday" ad.

The two ads also followed the typical pattern of showing patients who lost control of their lives as a result of their condition and how they regained control after treatment.<sup>171</sup> These advertisements often do not portray the average benefit of drug use, and also make suggestions about the drug that others dispute.<sup>172</sup> Although the Aricept advertisements do not present that all patients will benefit as the patients in the commercials have, they also do not describe the typical

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<sup>168</sup> *Id.*

<sup>169</sup> *Id.*

<sup>170</sup> *Id.*

<sup>171</sup> *Id.* at 12

<sup>172</sup> *Id.*

pattern of improvement or the possibility of the drug just slowing down progression of the disease. In these ways, DTC advertisements can distort and inflate expectations about the impact of the drugs on a condition.<sup>173</sup> The Aricept advertisements can give a false expectation that cognition and activity will return to normal, or at least improve, when it is probable that patients' Alzheimer's disease may just deteriorate at a slower pace.

The main differences between the patient insert and television advertisements relate to the balance between the positive and negative aspects of the drug. While the patient insert only has a brief section on benefits and outlines all potential effects of the drug, including no change, the television advertisement focuses at least half of its time on the before and after of a "best-case" scenario where the patient's condition actually improves. There is no discussion of the possibility that the drug will only slow progression. Furthermore, while most of the space for the patient insert discusses warnings and possible side effects, less than half of the television advertisement discusses such negative aspects of the drug. Lastly, even though the time devoted to factually describing the benefits of the drug may be comparable to the time devoted to describing risks and side effects, the visual images that are shown during the explanation of the risks and side effects are positive images of the patient getting better, which seem to further tip the balance of the advertisement towards the benefits. All of these are reasons that the television advertisement may give a more positive impression of the drug than the patient insert.

The FDA has taken actions against the manufacturer for two of its Aricept advertisements. The FDA sent a warning letter to Eisai Medical Research in 2010 stating that two Aricept television ads were misleading because they overstated the efficacy of the drug, thus leading to

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<sup>173</sup> *Id.*

Aricept being illegally misbranded.<sup>174</sup> The two commercials that the FDA found misleading are very similar in format to the two advertisements analyzed above, with the same pattern of a family member observing changes in the patient, the two of them visiting a doctor, and concluding with improvements in the patient's function.<sup>175</sup> Many of the criticisms in the FDA letter therefore likely apply to the two advertisements analyzed in this paper.

The letter focuses on the conjunction of the images of improved function and statements that Aricept can slow progression Alzheimer's symptoms and can improve cognition.<sup>176</sup> The problem seems to be that the behavior of the patients in the advertisements "changes dramatically" after the visit to the doctor.<sup>177</sup> In one advertisement, an elderly man who starts off looking disinterested is later shown "happily interacting" with family.<sup>178</sup> In the other advertisement, an aloof and confused elderly woman is later shown working on a garden with her daughter and grandchildren.<sup>179</sup> This is very similar to the Airport and Sunday ads where the confused-looking elderly patients are later seen interacting with their families after visiting the doctor. The FDA letter states that these claims and presentations misleadingly overstate efficacy because they imply that Aricept treatment can restore patients' cognitive and daily functioning to normal, when clinical trials do not support such a drastic improvement.<sup>180</sup> The FDA focuses on the visual images, rather than just the spoken parts, as it adds that including the superimposed text, "Individual results may vary," does not "mitigate" the misleading quality of the

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<sup>174</sup> FDA letter to Eisai, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM201238.pdf>

<sup>175</sup> FDA- Promotional Materials, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM201240.pdf>

<sup>176</sup> FDA letter, supra note 174.

<sup>177</sup> *Id.*

<sup>178</sup> *Id.*

<sup>179</sup> *Id.*

<sup>180</sup> *Id.*

advertisements.<sup>181</sup> Finally, the FDA requests that Eisai immediately cease the named advertisements.<sup>182</sup>

Although the FDA eventually did address problems with the Aricept advertisements, the warning letter came fourteen years after the approval of Aricept. Although the exact date that television advertising started is not clear, it is likely that such advertisements were on the air for several years before they were put to a stop. This suggests that enforcement actions, even when they do happen, do not come quickly enough to remove misleading advertisements from the public. Considering the scope of Alzheimer's disease, having such a television advertisement out for several years may have misled millions of viewers about the effectiveness of treatment.

Continued dissemination of misleading advertisements on the air is also not good for the pharmaceutical companies. Although they may initially have more patients due to increased demand for the drug, such advertising can lead to negative publicity. A simple internet search for "Aricept commercial" leads to links for parodies of the typical Aricept television advertisement,<sup>183</sup> and a search for "Aricept television advertisement" leads to news articles about the enforcement action against Eisai/Pfizer.<sup>184</sup> This also shows that a good portion of the public knows about and is interested in the Aricept commercials, which again supports the proposition that the FDA did not act quickly enough in removing these advertisements from dissemination.

Aricept is an example of an Alzheimer's disease drug which has been widely advertised through DTC advertising and has faced problems for its campaign. The effects of a misleading

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<sup>181</sup> *Id.*

<sup>182</sup> *Id.*

<sup>183</sup> *See, e.g.,* Alzheimer's! - An Aricept Commercial Parody, available at <http://www.youtube.com/watch?v=horzAQ8obAA>. The video appears to criticize the speed at which family members will attribute forgetfulness of elders to Alzheimer's disease.

<sup>184</sup> *See, e.g.,* Aricept TV spots hype benefits, says DDMAC, available at <http://www.mmm-online.com/aricept-tv-spots-hype-benefits-says-ddmac/article/164432/>.

advertisement can be very significant given the number of individuals affected by the disease and the number of their caregivers.

#### **IV. Next Steps and Proposals for Change**

Although there are many studies on the increased use of DTC advertising and its impacts on patient and physician perceptions, there is a lack of evidence of the impact of DTC advertising for specific drugs or fields of drugs. Given the projected increased prevalence of Alzheimer's disease, a study on the impact of DTC advertising on the usage of drugs to treat the disease and the overall costs and benefits of any changes in usage from such advertising may be beneficial. More specifically, studies similar to the Datti study could be conducted, but with a focus on whether Alzheimer's disease DTC advertisements affect the likelihood of increased drug prescription or the use of medical services in the older adult population. Furthermore, given the extra target of Alzheimer's DTC ads, a similar study could analyze the effects of the ads on family members requesting drugs or treatment on behalf of affected individuals, and whether this increases healthcare costs. A cost-benefit analysis is likely to be much more difficult, as it is challenging to assess psychological and other non-economic benefits from increased quality of life as a result of Alzheimer's disease treatment, but interviews of patients and caregivers could assess their satisfaction with pharmaceutical treatment and the rate at which they were dissatisfied by results due to high expectations from seeing DTC advertisements.

There are also many possibilities of reform for various sectors regarding DTC advertising in general and specifically for Alzheimer's disease. Given that prohibiting pharmaceutical advertising would likely be a violation of the First Amendment, most proposals for reform are

aimed at tighter regulation of DTC advertising by the FDA.<sup>185</sup> This includes development of more comprehensive standards, and an increase in funding so that the FDA can adequately review and enforce these standards.<sup>186</sup> Review of advertisements should focus especially on the visual elements, rather than on just the written or printed information.<sup>187</sup> As seen in the Aricept example, the visual portions of a television advertisement may mislead the audience. Even if they are not misleading, the visual images are often one-sided, and can upset the “fair balance” of the audio or spoken portions of the advertisement. Although it may not be practical to force manufacturers to visually show negative effects of a drug, more than half of the spoken part of a commercial could be devoted to risks to off-set the visual elements which are solely devoted to benefits.

Problems with DTC advertising often lie in the lack of information that the patient has, and there are other institutions which can support the FDA in providing more comprehensive information, such as the NIH and the AMA through its medicals schools and residencies.<sup>188</sup> Suggestions have also been made to supplement manufacturer advertising with public service messages which recommend consultation with physicians for certain conditions without reference to any specific treatment plan.<sup>189</sup> Also, the FDA could impose a moratorium on advertisement for a set period of time or under certain situations, such as for the first three years after initial market release of a drug.<sup>190</sup> The FDA should also educate the public as to the roles of

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<sup>185</sup> Sidney M. Wolfe, *Direct-to-Consumer Advertising- Education or Emotion Promotion?*, 346 N. Engl. J. Med. 524, 526 (2002).

<sup>186</sup> Hollon, *supra* note 44. Even the U.S. General Accounting Office has recommended that the FDA reduce the amount of time it takes for issuing regulatory letters. USGAO, *supra* note 40.

<sup>187</sup> Wilkes et al, *supra* note 6, at 124.

<sup>188</sup> Wolfe, *supra* note 185.

<sup>189</sup> Hollon, *supra* note 44 at 2032.

<sup>190</sup> *Id.*

promotional materials.<sup>191</sup> This will allow consumers to maintain a healthy skepticism towards DTC advertising.

These proposals can be shaped or adjusted depending on the type of drug being advertised. Given the special considerations of Alzheimer's disease discussed above, there could be special regulations pertaining to advertisements directed at family members of patients rather than patients themselves. Furthermore, education efforts would have to be addressed to the family in addition to the individual patient. This could involve special training in medical education for consultation with family or public service messages addressed to family members. As for a moratorium, a longer period of prohibition of advertisements for treatments of Alzheimer's disease may be appropriate than what is proposed above. This is because of the prolonged nature of both the disease and the recognition of any benefits from treatment.

Suggestions for reform have also been addressed to the pharmaceutical industry.<sup>192</sup> These include making advertisements more disease-centric than drug-centric, and encouraging nonproprietary partnerships with researchers to study the effects of DTC advertising and come up with strategies to more effectively communicate information to consumers.<sup>193</sup> Such changes would likely be helpful in the context of Alzheimer's disease. Since effective management of the disease can rely on more than a single type of treatment, a disease-oriented advertisement could lead to more effective use of medical treatment within a comprehensive regimen. Although such advertisements may not directly lead to use of a specific drug to treat the disease, they could lead to greater awareness of the disease which may result in more patients using medication to treat their conditions. Furthermore, enhancing consumer knowledge about the actual effectiveness of drugs could prevent heightened expectations from drugs which could lead to negative publicity

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<sup>191</sup> Wilkes et al., *supra* note 6, at 124.

<sup>192</sup> *Id.*

<sup>193</sup> *Id.*



or even litigation when a drug fails to meet those expectations. In these ways, the above mentioned reforms could even be helpful for manufacturers of Alzheimer's disease drugs.

The medical community, which often voices many of the criticisms towards DTC advertising and pharmaceutical manufacturers, should also be involved in reforming the system.<sup>194</sup> Studies have shown that primary care physicians are often the most skeptical towards DTC advertising.<sup>195</sup> As mentioned above, the medical community should be involved in informing the patient about available drug and non-medical therapies for conditions, as well as educating the public on the appropriate uses and limitations of medication.<sup>196</sup> At individual visits, physicians should not forego a thorough medical examination and succumb to pressure to prescribe medications for new conditions that patients come with as a result of watching a DTC advertisement.<sup>197</sup> With respect to Alzheimer's disease, there is a need to educate patients on the limits of the available drugs, especially since Alzheimer's is an incurable disease. There should be explanations on how the situations reflected in television advertisements may be a "best case" scenario so that patients and their families have a realistic view of what to expect from treatment.

DTC advertisements are likely here to stay. The FDA should continue to monitor and review these advertisements, especially for new treatments, so that the costs of increased prescription and use of expensive drugs do not outweigh the medical and social benefits of these medical therapies. The industry should also be cautious in not overstating the benefits of treatments, not just because of potential enforcement action by the FDA but also for publicity reasons and to have a more knowledgeable consumer base. Finally, the medical community should continue to educate patients of the true risks and benefits of various therapies while not

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<sup>194</sup> *Id.* at 125.

<sup>195</sup> *Id.* at 119.

<sup>196</sup> *Id.* at 125.

<sup>197</sup> *Id.*

ignoring patients who have brought a drug or condition to the attention of the physician because of a DTC advertisement. The number of cases of Alzheimer's disease will continue to increase as the population of America ages. Although the available therapies can only mitigate symptoms or slow down progression of the disease, any improvement on quality of life for patients and their caregivers can have a significant effect on public health and societal costs. There are many problems with the current state of DTC advertising of Alzheimer's disease drugs. However, abolition of such advertising is not necessarily the best solution in improving the health of the American public and economy. As long as the FDA effectively polices advertisements so that they do not overstate the benefits of such treatments, and patients and their families receive thorough and accurate information from a wide variety of sources, DTC advertising has the potential of bringing relief to millions of patients and caregivers whose lives are affected by Alzheimer's disease.