

## Online, Direct-to-Consumer Access to Insulin: Patient Safety Considerations and Reform

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### Abstract

The online, direct-to-consumer (DTC) medical marketplace is proliferating more rapidly than regulation is evolving to ensure proper patient safety and public health controls. Along with this growing body of unrestrained medical testing and pharmaceuticals offered DTC online, most types of insulin and insulin administration products may now be purchased without prescriptions or physician guidance. Given the relatively significant risks of insulin use, the abuse potential, the high prevalence of diabetes mellitus, and the rising population of uninsured and underinsured, it is imperative to reform the online DTC medical marketplace to ensure that patient safety and public health are protected.

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### Introduction

In 1941, insulin was the first medical therapeutic required by the U.S. Food and Drug Administration (FDA) to undergo a rigorous certification process to ensure batch safety before use in patient care.<sup>1</sup> However, in 1951, the initial prescription legend strangely exempted insulin from prescription status.<sup>2</sup> Some insulin types remain nonprescription today despite meeting two major FDA criteria for prescription-only status: (1) medications administered by injection; and (2) medications sufficiently toxic that patients cannot self-treat.<sup>2</sup>

Yet, although select insulin products in the United States are nonprescription, behind-the-counter status unofficially

restricts all insulin access.<sup>2</sup> Furthermore, the prescription-only status of syringes required to inject insulin has historically and indirectly limited access to the medication.<sup>3</sup> However, public health efforts since 2000 to deregulate insulin syringes<sup>3</sup>—also used by intravenous drug abusers—has resulted in the added consequence of reducing barriers to insulin use. Now, with the rapid proliferation of an online, direct-to-consumer (DTC) medical marketplace within a suboptimal regulatory environment, non-prescription insulin, prescription-only insulin, and syringes have all become available for online purchase without appropriate controls or medical-professional oversight. The significant clinical risks associated with

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**Abbreviations:** (DTC) direct to consumer, (FDA) U.S. Food and Drug Administration, (NPH) neutral protamine Hagedorn, (VIPPS) Verified Internet Pharmacy Practice Sites

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insulin use combined with unrestricted online DTC marketing and purchasing necessitates reform efforts in the interest of patient safety.

## Insulin and Risks

Severe hypoglycemia, which is defined as a hypoglycemic event requiring assistance of another person to actively administer carbohydrate, glucagons, or other resuscitative actions,<sup>4</sup> is the major risk associated with insulin use, and can result in death if untreated. An estimated 37–41% of patients with type 1 diabetes and 19% of patients with type 2 diabetes will experience severe hypoglycemia.<sup>5</sup> Several factors increase this risk: polypharmacy, concomitant use of betablockers or insulin secretagogues, hypoglycemia unawareness, alcohol use, and renal insufficiency.<sup>5</sup> Additionally, the only nonprescription insulins still approved for marketing by the FDA, which are neutral protamine Hagedorn (NPH), regular insulin, and 70/30,<sup>6</sup> carry greater risk of hypoglycemia compared with prescription-only insulins.<sup>7</sup>

Adding complexity to insulin therapy, an individual's insulin needs are unique to specific diet, activities, peripheral insulin resistance, pancreatic function, and physiologic particulars. Thus, it is impossible to know exact insulin dosing at therapy initiation and equally difficult to accurately assess and adjust insulin doses for changing health status, diet, and activities.<sup>6</sup> Indeed, various insulin formulations with differing therapeutic onset, peak-effect timing, and effect duration make titration of exact insulin needs extraordinarily complex, even for well-trained physicians.<sup>7</sup> In response to this complexity, primary care physicians generally tend to delay insulin use in patients with type 2 diabetes.<sup>6</sup>

In addition to the clinical risks, insulin is identified as a drug of abuse. Bodybuilders have abused insulin for its anabolic effects for many years.<sup>8</sup> Furthermore, insulin is widely documented as a murder weapon.<sup>8</sup> The unique clinical risks and abuse potential of insulin make it imperative to restrict inappropriate access.

## Insulin and the Online Direct-to-Consumer Medical Marketplace

Despite safety risks and abuse potential, the online DTC medical marketplace provides unfettered access to insulin without a prescription and without appropriate medical oversight. In fact, a simple online search for “insulin without prescription” reveals several vendors enabling purchase of many insulin products, including syringes,

Lantus,<sup>®</sup> Humalog,<sup>®</sup> Novolog,<sup>®</sup> Humulin,<sup>®</sup> Novolin,<sup>®</sup> and Vetsulin<sup>®</sup>. This availability specifically includes insulin products regulated by the FDA as prescription-only, as well as insulin types discontinued for human use, such as Vetsulin (**Table 1**). Many sites observed selling these prescription-only insulin products purport to be Canadian, a factor associated with increased risk of encountering counterfeit pharmaceuticals sourced from other countries.<sup>9</sup> Many observed websites also actively advertise delivery to the United States of insulin regulated by the FDA as prescription-only. Consequently, foreign websites explicitly engaged in promoting importation of prescription-only insulin to U.S. consumers are violating FDA regulations, which generally prohibit such importation. Furthermore, medications originating from foreign countries carry a higher risk of being counterfeit or being contaminated with toxic materials.<sup>9</sup> Finally, transportation oversight over any distance is particularly important for insulin because of the temperature-controlled conditions required to transport the medication.

Online availability of insulin products without prescriptions or medical-professional consultation poses serious risks to patients and consumers. First, the Internet eliminates the pharmacist-consumer safety counseling that takes place at brick-and-mortar pharmacies for both nonprescription and prescription-only medications. Second, even for patients well accustomed to their insulin regimens, an individual's insulin needs change over time and should

**Table 1.**  
Prescription versus Nonprescription Insulin in Various Countries

Country	Prescription Only	Nonprescription
Australia <sup>a</sup>	All	None
Italy <sup>a</sup>	All	None
Netherlands <sup>a</sup>	All	None
United Kingdom <sup>a</sup>	All	None
United States <sup>b</sup>	Apidra (glulisine) Humalog (lispro) Lantus (glargine) Levemir (detemir) Novolog (aspart) Novolog Mix (aspart/protamine) Humalog Mix (lispro/protamine)	Humulin R (Regular) Novolin R (Regular) Humulin N (NPH) Novolin N (NPH) Humulin 70/30 (70/30) Novolin 70/30 (70/30)

<sup>a</sup> U.S. Government Accountability Office. Accessed March 19, 2012. February 2009. Available at [www.gao.gov/htext/d09245.html](http://www.gao.gov/htext/d09245.html).

<sup>b</sup> U.S. Food and Drug Administration. FDA approved drug products. Accessed March 19, 2012. Available at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>.

be periodically monitored by medical professionals to ensure safety. Third, not realizing the differences in insulin types, patients may dangerously pursue Internet-based products and inadvertently or purposefully switch insulin types in response to cost concerns. Finally, access to the online DTC medical marketplace specifically threatens vulnerable patient populations, including young patients with type 1 diabetes who may lack access to coverage or who may be concerned about costs, the underinsured and the uninsured, and seniors who have reached their Medicare “donut hole” or are looking for more convenient ways to access treatments.

## Reform

Ideally, the FDA should regulate all insulin products as prescription-only, primarily because of the significant risk profile. Indeed, insulin fits the FDA definition for prescription-only medications, and newer insulin forms are classified as prescription-only (Table 1). In line with this reasoning, insulin is prescription-only in many other developed markets (Table 1). Achieving prescription-only status for all insulin products would empower the FDA to enforce the regulations and oversight requisite on entities selling and providing prescription-only medications in the United States.

Importantly, the unique risks posed by online sourcing of insulin require more nuanced regulatory action. Special rules should apply to insulin marketing and purchasing online given its professional guidance needs, high prevalence of diabetes mellitus in the United States, high incidence of adverse hypoglycemic events, abuse potential, existence of online counterfeit medications, potentially misleading DTC advertising, and illegality of personal importation of prescription-only insulin products into the United States. At a minimum, this should include limiting U.S. sales of insulin to online pharmacies accredited by the Verified Internet Pharmacy Practice Sites (VIPPS) program of the National Association of Boards of Pharmacy, the only online pharmacy accreditation endorsed by the FDA.<sup>10,11</sup> VIPPS accreditation would ensure that online pharmacies meet standard patient safety and insulin storage and transport requirements.<sup>11</sup>

Finally, the FDA should also critically assess online pharmacies and employ legal remedies against companies found to be engaging in illegal, fraudulent, or unlicensed activities. As with the recent Operation Pangea, law enforcement and international agencies should cooperate to target illicit online pharmaceutical vendors and high-

risk medications including insulin.<sup>10–12</sup> Operation Pangea is a public-private partnership involving entities from as many as 81 countries, resulting in confiscation of over 2.4 million counterfeit pills and shutting down of 13,500 illicit online websites that sell medications illegally.<sup>12</sup> While efforts to regulate illegal Internet-based activities have been notoriously difficult owing to blurry geopolitical borders, the Operation Pangea initiative could serve as a model for future public-private partnership initiatives specifically targeting online sales of high-risk pharmaceuticals, including insulin. A global solution involving various stakeholders would likely be more effective than a unilateral U.S.-centric approach to regulating dangerous prescription-only medications available online without a prescription. A systems approach to regulating online activities would help in reducing consumer risk while also preserving online access to legitimate insulin therapy products for consumer benefit.

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