Overpatented, Overpriced

Imbruvica's Patent Wall

ISSUE: While there are many causes of high drug prices, perhaps the least recognized is the connection to the patent system. In particular, there is little understanding of the specific patent strategies employed by drug makers and how these strategies impact competition.

GOAL: Investigate the patent strategy used for the cancer drug Imbruvica in order to better comprehend how "patent walls" are constructed.

METHODS: Identify all patents related to Imbruvica and analyze them to determine which types of patents were filed, when they were filed, and how this filing pattern impacted the length of time the drug would be protected by patents.

KEY FINDINGS:

- Imbruvica has **165 patent applications;** to date 88 patents have been granted.
- **55%** of the patent applications on Imbruvica were filed **after its first FDA approval.**
- **58%** of patent applications cover the different indications and formulations of the drug, **not the active substance itself**.
- Granted patents protect Imbruvica's commercial **exclusivity for 29 years.**
- The estimated **spending** on branded Imbruvica during the nine years of extended exclusivity is **at least $41 billion.**

CONCLUSION: Our analysis of Imbruvica reveals a "drip feed" patenting strategy. The initial patent applications on Imbruvica cast a wide net of scientific knowledge and protection, including potential indications and formulations. This knowledge is then disaggregated and patented in phases with more specificity. Because the current patent system is one-size-fits-all—all patents are rewarded with the same 20-year period of exclusivity—the additional granted patents on Imbruvica to date have lengthened its patent protection by nine years. This raises important questions about patent standards, rewards, and incentives.

Revised July 2020

Results

The majority of Imbruvica patents were filed after the drug was brought to market

For the purpose of this brief, we use the term **patent wall** to describe the portfolio of patents relating to a single drug. Imbruvica's patent wall includes the 165 patent applications that have been filed on the drug as of November 2019. The first application on Imbruvica was filed in December 2006 and the most recent was filed in September 2019, a span of 13 years. **88 patents have been granted** on Imbruvica (53%),[6] 37% have been abandoned (see *Abandoned Applications* below), and 9% are still pending a decision. **Granted patents protect Imbruvica's commercial exclusivity for 29 years**, from December 2006 to March 2036**.**

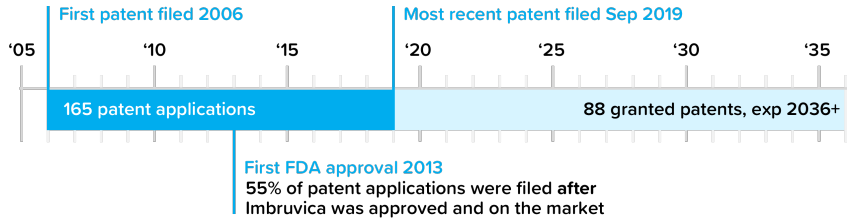


Figure 1: Imbruvica's patent lifecycle

It is commonly accepted that patents are needed to incentivize the investment required in order to bring a new drug to market. However, patenting activity did not stop once Imbruvica was launched. In fact, **55% of patent applications for Imbruvica were filed after the drug was approved by the FDA** in November 2013 and brought to market. This raises questions about other factors, including commercial ones, driving a company's ongoing pursuit of patents.

Key facts about Imbruvica

Indications: A small molecule drug used to treat a variety of B cell cancers, including leukemia and lymphoma.

Manufacturer: Developed and put into clinical trials by Pharmacyclics beginning in 2006. Pharmacyclics was acquired by AbbVie in mid 2015.

FDA Approval: First approved in November 2013.

Price: Current non-discounted annual price is $174,156.[1] The price has increased over 57% in the five years since the drug was launched.[2] In the month of January 2020, its price increased by over 7%.[3]

Public Spending: Total net spending in the U.S. has exceeded $15 billion in the six years since its approval, with average annual growth of 56% in the past four years.[4]

Forecast: By 2024, projected to become the fourth highest grossing drug in the U.S., with annual revenues of nearly $9 billion.[5]

[1] For the most widely used 140mg oral capsule, 90 capsule (one-month supply). https://www.drugs.com/price-guide/imbruvica
[2] Based on AWP for 140mg capsule, 120 per package, from Jan 1, 2014 to Jan 1, 2019
[3] Patients for Affordable Drugs. January 2020 Price Hikes: Imbruvica. 8 Jan 2020. https://www.patientsforaffordabledrugs.org/2020/01/08/imbruvica/
[4] From an analysis of the annual and quarterly reports of AbbVie and J&J from 2014-2019. Actual figures for Q4 2019 are not yet available and are estimates.
[5] EvaluatePharma World Preview Report. Table 14: Top 10 Selling Products in the USA in 2024. May, 2019.
[6] 31 granted patents are listed on the U.S FDA Orange Book

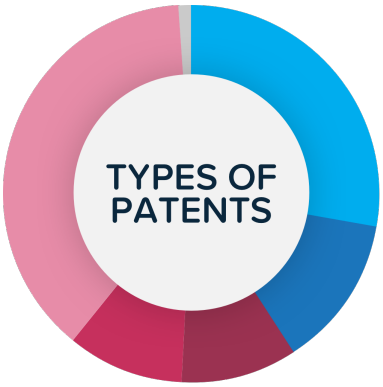
ABANDONED APPLICATIONS: Patent applications that are voluntarily discontinued by an applicant are classified as abandoned. However, it is common for the subject matter contained in abandoned applications to appear in other patent applications or granted patents. This is because the patent system permits applicants to file "continuation applications," which are the re-filing of patent applications previously rejected by the U.S Patent and Trademark Office (USPTO) or that seek to add additional protection for subject matter already covered by an earlier filing or granted patent. The procedure can be used to indefinitely prolong examination of a patent application until a patent is obtained or the applicant voluntarily withdraws the application.[7] This makes it difficult for the USPTO to definitively reject a patent application during examination.[8]

The majority of the patents in Imbruvica's patent wall cover indications and formulations—not the active substance

The active substance is what provides the therapeutic or medicinal benefit of a drug. Indications and formulations refer to the conditions a medicine can be used for and how it is taken (a tablet or a capsule, for example). Patents covering the active substance are often referred to as "primary patents" and typically reflect the main medical and scientific advancement on a drug. Patents on indications and formulations, called "secondary" patents, usually cover sub-components of the main invention described in the primary patent.[9]

Secondary patents constitute 58% of Imbruvica's patent wall; 42% cover the active substance and its derivative compounds.

Figure 2:
The types of patents in Imbruvica's patent wall



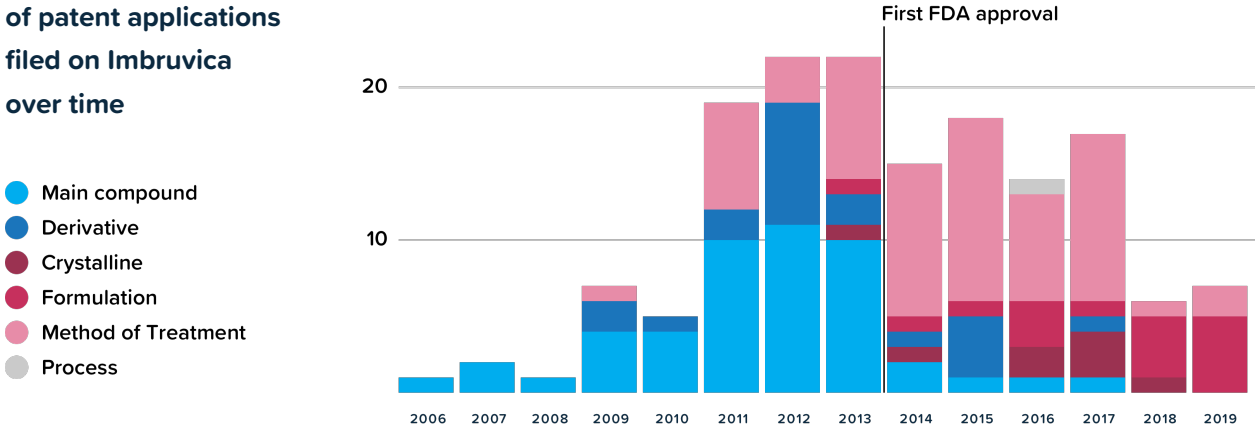
- **Main compound (28%):** Covers the active substance used in the marketed drug. Base patents typically have the broadest scope.
- **Derivative (13%):** Structural variations of the main compound are filed as part of the main patents for the broadest protection.
- **Crystalline (10%):** Crystal structures inherent within the main compound, and can vary in their physicochemical properties (does not change biological properties).
- **Formulation (10%):** Pharmaceutical preparations used to administer the product (e.g. tablet, transdermal patches).
- **Method of Treatment (38%):** Specific indications (diseases) that can be treated with the main compound alone or with another active substance(s).
- **Process (<1%):** Methods for preparing the main compound, derivative, crystalline form(s), or formulations for manufacture.

[7] C Chen. Using Continuation Applications Strategically. Cooley Go. https://www.cooleygo.com/using-continuation-applications-strategically/
[8] MD Frakes and M Wasserman. Decreasing the Patent Office's Incentives to Grant Invalid Patents. The Hamilton Project. Dec 2017. https://www.hamiltonproject.org/papers/decreasing_the_patent_offices_incentives_to_grant_invalid_patents
[9] The European Commission. *Pharmaceutical Sector Inquiry Final Report.* Rep. European Commission. 2009. P. 180

Imbruvica's Patent Wall Suggests a "Drip Feed" Patenting Strategy

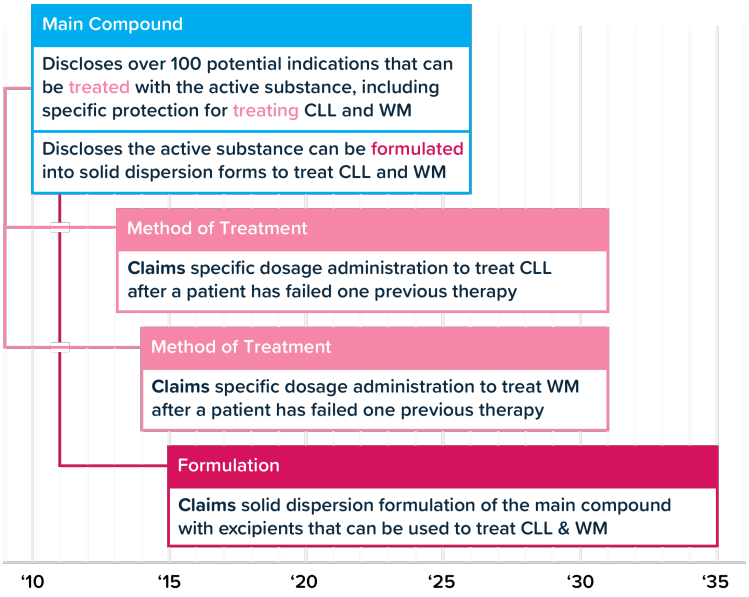
As seen in Figure 3, the majority of patent applications filed prior to the first FDA approval are for the active substance and its derivative compounds. In the three years prior to FDA approval in 2013, there is a marked increase in the number and type of patent applications. This increase reflects patent applications seeking to protect aspects of the main compound or its derivatives that were not specifically protected in the first phase of applications. It also includes secondary patent applications specifically claiming certain indications and formulations, including a crystalline compound. Following the first FDA approval in 2013, further secondary patent applications continued to be filed for additional indications and formulations and/or to describe elements of earlier patents more specifically.

Figure 3: The types of patent applications filed on Imbruvica over time



Our analysis reveals a pattern of patenting in which knowledge related to an invention is "drip fed" out over time. That is, knowledge broadly disclosed in early patent applications is defined ever more narrowly and specifically in subsequent patent applications.

For example, one main compound patent broadly describes more than one hundred possible indications for Imbruvica, as well as potential formulation routes. It also seeks protection for several defined indications. Three additional patents were subsequently filed that further specified aspects of the main patent.



WM = Waldenstrom macroglobulinemia. **CLL** = Chronic lymphocytic leukemia.

Figure 4: Example of the "drip feed" patenting strategy

Two of these patents protect the active substance for indications that were disclosed and protected by the main compound patent, but with the addition of a specific oral dose for a subpopulation who have failed at least one therapy. The third patent specifically protects how to formulate the active substance for treating CLL and WM using common techniques already described in the main compound patent. These three additional patents extend five to nine years beyond the main compound patent, expiring in 2031–2035.

We found this kind of "drip feed" strategy, in which knowledge was disaggregated and then distributed over time with more specificity, employed across Imbruvica's patent portfolio. **Early patents on the main compound served as a roadmap for future patenting activity**, signaling the potential for multiple different indications, formulation types, crystalline forms, combinations with other active substances, prodrugs, and more, while leaving enough room for subsequent patents to define these details more precisely. This raises important questions about what was known at the time of filing on the main compound and whether certain scientific findings were staged to lengthen the monopoly term given current patent law allows for such practices.

Patents on indications and formulations of Imbruvica lengthen its monopoly term 9+ years and Americans will incur at least $41 billion in spending

As noted earlier, patent applications on Imbruvica have been filed over the course of 13+ years. Specifically, method of treatment and formulation patents were filed later in Imbruvica's patent lifecycle, and therefore **extend commercial exclusivity more than nine years** beyond the expiration of the initial patent. During that time, Americans will spend an **estimated $41 billion on branded Imbruvica.**[10] This calculation is based on granted patents identified as of November 2019. We anticipate that more patents will be filed and granted on this drug.

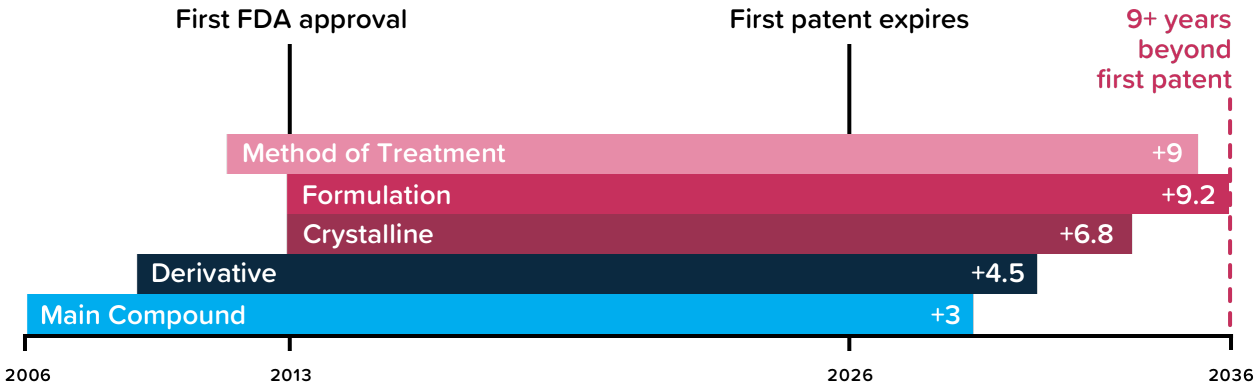


Figure 5: How the types of granted patents extend the patent term on Imbruvica

[10] Based on an I-MAK model of estimated revenue/spending for Imbruvica in the ten-year period from 2027–2036. Assumes total U.S. revenue for Imbruvica increases until 2024 when it reaches a peak of $8.7B ($6.2B AbbVie and $2.5B J&J), which is consistent with various market forecasts (see EvaluatePharma, May 2019). From 2025 onward, the model conservatively assumes there are *decreases* of 10% annually in total U.S. revenue/spending through 2036, based on new products entering the market and reduced market share for Imbruvica. There is no assumption of a generic product entering the market in this time period.

Conclusion

This analysis raises important questions for policymakers who are searching for impactful solutions to the drug pricing crisis.

The current one-size-fits-all patent system enables the "drip feed" patenting strategy seen in Imbruvica. The first patent on the main compound and subsequent patents all receive the same 20 years of exclusivity, regardless of what was already known at the time the first patent was filed.

As a result, pharmaceutical companies can file initial patents quite broadly and then file separate, subsequent patents on aspects of the original invention. In many cases, these later patents reveal marginally more information or specificity than earlier patents. Nevertheless, companies are able to substantially extend monopoly terms using this strategy. **As long as subsequent patents are written specifically enough to be considered outside the scope of disclosure of the first patent(s), the potential to keep stacking additional patents on a single, already patented active substance is limitless**.

Supplementary material for this report, including the methodology, is available at **i-mak.org/imbruvica**

Policymakers addressing rising drug costs can consider the following key questions related to current patent law:

1. **Are the standards for what is considered inventive too low** and **does Congress need to redefine the types of inventions that deserve a patent?** This would include redefining what is novel and non-obvious.
2. **Does the current standard for invention create incentives for companies to extract as many patents as possible** on a single active substance in order to prolong the monopoly period?
3. **Should subsequent patents be considered inventive** if they cover subject matter that were already disclosed in the first patents?
4. **Does the current "drip feed" patent strategy represent a loophole in the patent system** that is allowing drug makers to extend their monopoly protection?