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# Januvia Generics Arrive: Can MSD Defend Its Turf In India?

*Sitagliptin Looks To Unseat Teneligliptin, Vildagliptin*

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A wave of cut-price sitagliptin generics is seen hitting the Indian market with expiry of the patent on Merck's Januvia, a product that has had a hugely eventful journey over the years including fending off pre-expiry challengers. Will the company respond with price cuts?

Dozens of sitagliptin generic brands are expected to swarm the Indian market in the days to come with [Merck & Co., Inc.](#)'s blockbuster diabetes drugs, Januvia (sitagliptin) and Janumet (sitagliptin/metformin hydrochloride) losing patent cover this month in the country.

Among the first off the block is nemesis and past Januvia challenger, [Glenmark Pharmaceuticals Limited](#), which has introduced the dipeptidyl peptidase-4 (DPP-4) inhibitor at a fraction of the cost of the innovator product and also a combination with dapagliflozin. The Indian firm and MSD, as Merck & Co is known outside of the US and Canada, had been engaged in a hotly contested legal battle in the past after the former mounted a pre-expiry challenge to Januvia. (*See side box*)

Glenmark's Sitazit (sitagliptin) 50mg is available at INR10.5 (\$0.13) per tablet,

## **The Januvia India Story**

Merck's blockbuster diabetes drugs, Januvia and Janumet have had an eventful journey in India, one that perhaps encapsulates what it takes to compete in a complex out-of-pocket emerging market.

From going through with a bold India-specific pricing approach for a patented drug way back in 2008 to fending off a local pre-expiry patent challenge after a fiercely contested legal battle, Januvia/Janumet now face an

with the 100mg strength priced at INR14.5 per tablet versus Januvia's corresponding price of around INR37.8 and INR41.4. Sitazit-M (sitagliptin 50mg + metformin 500mg) is available at INR12.5 per tablet compared with about INR23 for Janumet 500 with similar differentials seen for Sitazit M (sitagliptin 50mg + metformin 1000mg) and Janumet 1000. In addition the Indian firm has Sitazit-M ER, an extended release version of the sitagliptin/metformin combination as well as two variants of Sitazit D, a combination of sitagliptin and dapagliflozin.

Others in the fray with Januvia generics include erstwhile MSD partner [Sun Pharmaceutical Industries Ltd.](#), [Zydus Lifesciences Limited](#), [JB Chemicals & Pharmaceuticals Ltd.](#) and others such as [Emcure.](#), Exemed, Morepen, [Alkem Laboratories Ltd.](#) Zydus said that its sitagliptin brands Sitaglyn and Siglyn will provide access to quality care to patients at an affordable cost with its brands approximately 60% lower than the originator product.

### Sitagliptin To Unseat Other Gliptins?

Industry experts anticipate a first wave of around 50 players to vie for a share of the sitagliptin pie in India. More importantly they see a shift in the pecking order in the DPP4 inhibitor market, with sitagliptin displacing teneligliptin as the preferred therapy and some experts going as far as saying that it could overtake vildagliptin.

Pricing for generic plain sitagliptin is

avalanche of cut-price generics coming their way following patent expiry this month in India. (Also see "[Pre-expiry Januvia generics may test Merck's resolve in India](#)" - Scrip, 28 Mar, 2013.) (Also see "[Merck Wards Off More Januvia Infringers In India](#)" - Scrip, 4 Nov, 2015.) (Also see "[MSD takes Glenmark to court over sitagliptin 'infringement'](#)" - Scrip, 3 Apr, 2013.)

The diabetes therapies were among the early products that MSD introduced in 2008 in India at differential prices – Januvia was at the time said to be available at about INR43 per day in India, compared to around \$5 a day (equivalent to INR200 then) in the US.

The strategy, was seen as game changer of sorts for Merck as it sought to expand access to the DPP-4 inhibitor in India, which currently has an estimated 74 million adults living with diabetes. The US firm also entered into a co-marketing arrangement with Sun Pharmaceutical Industries for the products to further propel these efforts.

The story behind the pricing stance for Januvia has some interesting nuances. The US firm apparently undertook multi-forked India studies on attributes of the product versus pricing covering diabetes patients, physicians and caregivers and did a price- volume analysis thereon that threw up interesting findings - the long-term sustainable price was seen to be in the range of around INR40-45.

While that was considered “the rock bottom

expected to trend in the INR8-10 per tablet range, with that of sitagliptin + metformin combination seen in the INR12-22 range, they added. There is a price cap component apparently to be dealt with, after India's National Pharmaceutical Pricing Authority fixed prices of sitagliptin and metformin combinations of several firms in May this year - further updates on this, if any, could not immediately be ascertained.

“Sitagliptin should unseat teneligliptin given that it is a better molecule than some of the leading gliptins and comes with robust clinical data; it should capture much more share of voice hereon,” an industry expert with vast experience in the diabetes segment across companies told *Scrip*.

IQVIA moving annual total (MAT) data for May indicated that for plain DPP-4 inhibitor molecules, teneligliptin leads the pack, followed by vildagliptin, linagliptin and then sitagliptin. However, when it comes to DPP-4 inhibitors plus metformin, the vildagliptin combination leads the pack with sitagliptin/metformin in second position and teneligliptin/metformin in third spot as per the data. (Also see "[Competition Piles Up: 100 Teneligliptin Brands Now In India](#)" - *Scrip*, 16 Oct, 2017.)

The overall Indian DPP-4 inhibitor (considering plain as well as metformin combination together) market is valued at INR36.21bn (\$457m) and is growing at 2.2% as per IQVIA TSA [total sales audit] MAT data for May 2022. The market for

story [ given the US, Europe prices of Januvia at the time]”, as one source in the know put it, what surprised the company was the level of shift that physicians were ready to make towards sitagliptin because of their style of practice which was, among other aspects, geared around minimizing the risk of hypoglycemia. With the DPP-4 inhibitor class offering a range of other benefits, physicians appeared ready to think about a price which was higher than the normal treatment cost and also perhaps saw the drug as “a bridge” between treatments available at the time and “insulinization”.

Indications are that the Indian pricing plan took considerable convincing to do at the US firm - it is believed to have gone all the way to Richard Clark, chairman of Merck & Co at the time - and was finally green-lighted amid promise of sharp volumes and cumulative sales expectations of around \$100m some years down the line .

“Never before had any diabetes product launch seen such sales volumes in India,” an industry expert recalled.

### Sitagliptin Pre-Expiry Challenge

But in 2013, Merck appeared to have been caught off-guard when domestic company Glenmark introduced its cut-price version of Januvia and Janumet on the Indian market ahead of the expected patent expiry date. Glenmark's brands Zita and Zita-Met were priced 30% lower. *Scrip*, at the time, was the

plain DPP-4 inhibitors stood at INR12.25bn during the period contributing 34% of the total, but has been stagnant in terms of growth whereas the DPP-4 inhibitor + metformin combination market, which contributed 66%, reflected growth of 3.2% at MAT level, the data indicated.

IQVIA data suggests that growth in the DPP-4 inhibitor market is essentially due to vildagliptin and vildagliptin+ metformin combination, with the other gliptins either stagnant or having reflected de-growth within the segment.

## MSD To Continue Deliver The 'Highest Quality Products'

Meanwhile, MSD has asserted that it remains very much in the game for sitagliptin in India.

Industry experts quoted previously expect the US firm to lower the price of Januvia by around 20-30% to compete in the segment and maintained that the brand has a "huge recall".

"There will still be a section of physicians who will feel much more comfortable using the MSD brand, price notwithstanding; the company should be able to hold on to reasonable volumes," one expert asserted to *Scrip*.

Others also referred to how MSD has perhaps been ahead of the game in some ways by using local manufacturing - via Recipharm Pharmservices Pvt Ltd in Bangalore - for the DPP-4 inhibitor well in advance, though this could not immediately be verified.

first to report Glenmark's actions.

While the Indian firm claimed that Zita and Zita-Met were "non-infringing", Merck said that it believed they "directly infringe" upon its intellectual property.

What followed was a high decibel court battle, with Merck asserting that as an innovative pharmaceutical company, protection of its intellectual property is vital to ensuring that "we continue to assume the tremendous monetary risks associated with the discovery of innovative medicines".

The case went MSD's way and in October 2015 the Delhi High Court issued a permanent injunction against Glenmark's cut-price versions of Januvia/Janumet. (Also see "[Permanent Indian Bar Against Glenmark's Sitagliptin Copies](#)" - *Scrip*, 8 Oct, 2015.) Among a string of observations, the judge held that MSD had succeeded in proving that the suit patent discloses sitagliptin phosphate monohydrate "generically."

Interestingly, 2015 also saw Glenmark launch another DPP-4 inhibitor teneligliptin, a cut-price version of [Mitsubishi Tanabe Pharma Corporation's](#) Tenelia, in India via a dual brand approach and at a price point that was approximately 55% lower than the other DPP4 inhibitors available in India at that time. (Also see "[Glenmark 'pioneers' Mitsubishi's teneligliptin in India](#)" - *Scrip*, 15 Jun, 2015.)

MSD did not specifically comment on plans to reduce prices of Januvia but underscored to *Scrip* that it will continue manufacturing, marketing and distribution of sitagliptin and sitagliptin combinations in India and continue to hold the rights to its brands Januvia, Janumet and Janumet XR CP.

“We will also continue to deliver the highest quality products and services. MSD is committed to the patient-first approach and our goal remains to make our medicines and vaccines available to people so they can live longer, healthier lives,” the US firm said.

It further clarified that beginning 6 July 2022, its co-marketing partnership with Sun, “which is greatly valued”, has come to an end. “Going forward Sun would be manufacturing and distributing the secondary brands on their own,” MSD said.

Sun, which is India’s top-ranked drug firm, had been co-marketing sitagliptin as Istavel and the sitagliptin +metformin combination under the brand name Istamet under its alliance with MSD.

### **Global Januvia/Janumet Patent Expiry**

The influx of generics in India comes ahead of anticipated patent expiry of the money spinner type 2 diabetes therapy in other markets.

Januvia and Janumet are expected to lose market exclusivity in the US in January 2023, in the EU in September 2022 and in China this month. The products reported global sales of about \$5.3bn in 2021.

Merck expects sales of Januvia and Janumet in these markets to decline “substantially” after the loss of exclusivity, it said in a filing with the US Securities and Exchange Commission in February this year. However, Januvia, Janumet, and Janumet XR contain sitagliptin phosphate monohydrate and the company has another patent covering certain phosphate salt and polymorphic forms of sitagliptin (2027 salt/polymorph patent), which, if determined to be valid, would preclude generic manufacturers from making sitagliptin phosphate salt and polymorphic forms until 2027 with the expiration of that patent, plus pediatric exclusivity, the US company said in the filing.

Par Pharmaceutical had in 2019 filed a suit in the US seeking a declaratory judgment of invalidity of the 2027 salt/polymorph patent. Merck responded with a patent infringement lawsuit against the firm and some other companies that also indicated an intent to market generic versions of Januvia, Janumet, and Janumet XR following expiration of key patent protection, but prior to the expiration of the 2027 salt/polymorph patent, and a later granted patent covering the Janumet formulation where its term plus the pediatric exclusivity ends in 2029.

Merck has since settled with 21 generic companies, which can launch their generic versions of

Januvia and Janumet in May 2026 or earlier under certain circumstances, and similarly their generic Janumet XR in July 2026, details in the SEC filing said.

There are other litigations as well including action by generic companies that have sought revocation of the Supplementary Protection Certificate for Janumet in certain European countries; if these firms are successful, Janumet could lose market exclusivity in these countries at the same time as the expiry of Januvia pediatric market exclusivity in September 2022, Merck said in a May filing with the SEC.