Big chase for a cancer drug: The urgent need for affordable Keytruda alternatives

Keytruda, a cancer treatment drug, has achieved $25 billion in global sales. Its mechanism boosts the immune system to fight cancer. In India, its high cost limits access. With patents expiring soon, Indian companies are developing more affordable versions. Efforts are also focused on expanding indications and improving financial access.

Mumbai/New Delhi : USD 25 billion or Rs 2.1 lakh crore. That's the worldwide sales figure of a single drug called Keytruda (its generic name is pembrolizumab). Keytruda, which is used to treat multiple forms of cancers, is the biggest blockbuster in the history of medical research. For a perspective, $25 billion is the size of the entire Indian pharmaceutical market. It is roughly five times the sales of India's biggest drug maker, Sun Pharma.

Unlike most medicines that treat a few indications or medical conditions, Keytruda is approved in the US to treat 40 cancers. In India, it is approved for use in 17 indications across 10 cancers or tumour types. Oncologists mostly prescribe it to treat certain types of lung cancers, followed by gastrointestinal cancer, triple-negative breast cancer and head and neck cancers.

For all cancers, Keytruda's mechanism of action or the way it works is simple and yet ground-breaking. It helps the body's immune system, which is the T-cells, to detect and fight cancer cells that hide and spread in organs.

PD-1 (programmed cell death protein 1) and PD-L1 (programmed deathligand 1) are proteins that act like armour and protect cancer cells from destruction by T-cells. After the infusion, Keytruda binds to the proteins, thereby activating the immune system that overpowers cancer cells, leading the tumours to shrink. It nudges the body's inherent defence mechanism to take on the invading cells. That is the reason why Keytruda and other drugs like Opdivo (nivolumab) of Bristol Myers Squibb are categorised as immunotherapy drugs.

A leading scientist in an Indian company draws a simple analogy. He says once the infusion starts to work at the tumour site, it liberates the army (immune system) from the prison, which then takes up the role of attacking the enemy (cancer cells). That's a gamechanger in precision medicine research unlike the extensively used chemotherapy drugs that kill cancer cells but also damage healthy ones.

However, Keytruda's prohibitive pricing—a couple of lakhs of rupees for a dose—has kept it out of reach of most patients in India. As its pharmaceutical company Merck's initial patents are set to expire in a few years, Indian drugmakers are racing to make affordable versions of it.

BIG SHOT

The resounding impact of Keytruda has been visible from the time it was launched in the US in 2014. A year later, Keytruda was used to treat former US president Jimmy Carter, who was detected with end-stage metastatic melanoma, a deadly form of skin cancer that had spread to his brain and liver.

Infusions over the next few months saw Carter gain health and become free of cancer. He turned 100 earlier this month. Patients getting out of cancer, like Carter, is the Holy Grail.

Keytruda, even if in a few cases, is proving to be just that and while all are not as lucky as Carter, oncologists are unequivocal about how a single drug changed the way the disease has been perceived. It has been "the Emperor of All Maladies", as the title of a book by the oncologist Siddhartha Mukherjee goes. But cancer is no longer, not always, a death sentence.

The global sales of Keytruda have set Merck's cash registers ringing. Its sales have doubled from five years ago. Last year's $25 billion was close to half of Merck's annual sales of $60 billion.

At a recent conference, Merck's global CEO Robert Davis noted the company has spent $60 billion so far in developing Keytruda and it expects to invest another $20 billion by 2030. Sachin Trivedi, director, medical oncology, HCG ICS Khubchandani Cancer Centre in Colaba, Mumbai, says Keytruda is an example of how an in-depth understanding of the biology of cancer and modern medicine can come together to create a miracle.

Diseases such as melanoma, which were thought to be incurable, have been controlled. "It is a shining example of a modern medical miracle," he adds.

Roshni Dasgupta, consultant medical oncologist, HCG Cancer Centre, Bengaluru, agrees. Keytruda works best with positive biomarkers (a test that precisely shows on which type of patients the drug may work) and even without biomarkers, in a few cases, when used along with chemotherapy.

"The response is excellent with 40- 60% achieving complete or partial remission, subject to tumour site and stage of the disease," she says. Dasgupta says another 25-30% have stable disease in a metastatic setting, which is the condition where cancer cells spread to other organs. While these are median survival rates diagnosed in patients at advanced stages, cancer is a disease that brings the extremes of hope and despair.

A Delhi-based doctor says one of his patients is in remission for seven years after using Keytruda but there are also those who may not have made it. An elderly patient's daughter based in Delhi told ET that the drug has not shown a desirable change after three cycles. The family have their hopes pinned on the next two cycles.

Meenu Walia, vice chairman, medical oncology, Max Super Speciality Hospital, New Delhi, says she has seen some miraculous results. "Patients, who would not have survived for more than five-six months, have been doing well for years. There is no exact percentage and there is no way one can predict the survival rate but, in some cases, it has worked wonderfully."

However, Keytruda is also known to sometimes cause the immune system to attack organs and tissues. When severe, that can be life-threatening.

COST BARRIER

The big hurdle for patients to access the drug is its humungous price. For Keytruda, the patient pays roughly Rs 2 lakh for each dose. Even though it is a fraction of the US costs, it is a significant barrier for a large swathe of patients in India, who mostly pay out-of pocket and are not covered under any health insurance.

Health policy experts have lobbied for long with the government to find ways to prevent a single cancer incident from plunging an entire family into financial catastrophe. The moral dilemma for doctors like Walia is to see the helplessness of patients who cannot afford the drug even when they could benefit from it.

Walia says MSD (as Merck is known outside of US and Canada) provides one dose free to qualifying patients along with their first dose. After five doses, it provides free doses for a year on the condition that the drug is prescribed by a doctor, patients are financially compromised and respond to the treatment.

Rehan Khan, MD, India Region, MSD, says the goal is to make pembrolizumab accessible to many more patients by expanding the number of approved indications and improving financial access to the therapy. Only three indications of Keytruda were approved in 2020 in India but he says these have been expanded to 17 indications and 10 tumour types.

"We will continue to focus on serving patients with our innovations," says Khan, adding that he believes it is important to pursue additional patient benefits through innovation. Globally, Merck is exploring hundreds of studies, probably the highest, combining Keytruda with other formulations to sharpen its effectiveness. There is also intense work on a subcutaneous form of Keytruda, which is expected to make it convenient for use and save time and costs for patients going to hospital for infusions. But that also means Merck can extend its patent life on Keytruda by several years.

INDIAN COMPANIES IN THE RACE

Experts say the solo run of Keytruda is expected to end in less than four years, at least partially. The first set of patent protection is likely to expire in Europe in 2028. Since patents in the US are granted on the basis of each additional indication filed, the patent protection for Keytruda in the country stretches until 2036. The hint of opportunity has sent a bunch of ambitious Indian drugmakers into action mode. They are bracing for a launch of biosimilars or near-copies of Keytruda.

For patients, that's good news as any launch of a biosimilar pembrolizumab is expected to cut the prices by at least 30-40%. By conservative estimates, the first wave of biosimilars is expected to be launched in India at half the current prices and, as competition picks up, a steady drop will follow.

While global giants like Korean companies Samsung Bioepis and Celltrion, Switzerland-based Sandoz and US-headquartered Amgen have announced big strides in the drug, leading Indian drugmakers are remaining quiet but sure-footed before making a splash. ET has learnt that at least six drug makers from India are at various stages of research for biosimilars of Keytruda but have yet to disclose their plans due to competitive reasons.

The big names include Biocon Biologics, Mumbai-based Ipca Laboratories, Enzene Biosciences (the biotech contract research and manufacturing arm of Alkem), Zydus Lifesciences, Dr Reddy's Labs, Mankind Pharma and Sun Pharma. Questions to these companies did not receive a response except for Biocon Biologics.

A spokesperson from Biocon Biologics told ET that the company does not disclose the names of assets until they have moved to late-stage development. “Hence I am not in a position to confirm or deny whether we are developing a biosimilar for Keytruda or if biosimilar pembrolizumab is a part of our biosimilars pipeline,” the spokesperson says in an emailed response. Making Keytruda needs years of expertise in biotechnology drugs.

The manufacturing complexity requires a heavy investment of at least Rs 100 crore and that is where the competition gets tough. Keytruda is a monoclonal antibody or a drug developed from living cells, which works by binding to a protein or a target to either fight it or stop it from causing damage to other cells.

Such drugs involve a maze of upstream and downstream processes, like generating cell lines, cloning them as close to the original drug, purifying and scaling it to accuracy in large bioreactors exactly as they were in the lab stages. Walia has another worry. She says though Keytruda is a complex biologic, the risk of counterfeits or substandard imports exists in India.

Many patients could fall prey to such counterfeits and end up losing money and lives. Her sage advice for patients and healthcare providers is to be vigilant and verify the sources from which such drugs are purchased, mostly lesser-known suppliers or online platforms.

As of now, the problem of counterfeit Keytruda in India is not widespread, but Walia says the high cost of immunotherapies does make it a target for illegal market. While the biosimilars are not expected before the patent expires in the next four years, the flourishing counterfeit racket brings an element of urgency for an authentic and cheaper variant for cancer patients. It could make the difference between life and death like for Jimmy Carter.

News Source:

https://pharma.economictimes.indiatimes.com/news/pharma-industry/big-chase-for-a-cancer-drug-the-urgent-need-for-affordable-keytruda-alternatives/114647704?utm_source=whatsapp_web&utm_medium=social&utm_campaign=socialsharebuttons