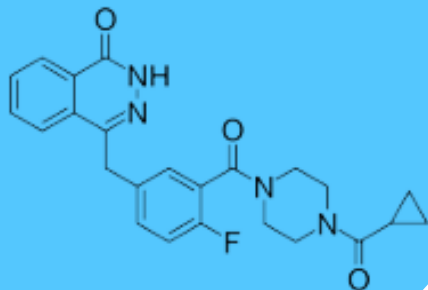


Olaparib



Olaparib API

Chemical Name:

4-[[3-[4-(cyclopropanecarbonyl)piperazine-1-carbonyl]-4-fluorophenyl]methyl]-2H-phthalazin-1-one.

Chemical Formula: C₂₄H₂₃FN₄O₃

Olaparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostases, such as DNA transcription, cell cycle regulation, and DNA repair.

Olaparib is indicated:

1. As monotherapy in patients with deleterious or suspected deleterious germline.
2. BRCA (breast cancer gene) mutated (as detected by an FDA-approved test) or advanced ovarian cancer after three or more prior lines of chemotherapy.

Lynparza® is the leading PARP (poly (ADP-ribose) polymerase) inhibitor approved in over 64 countries to treat ovarian cancer and in 40 countries for breast cancer. Below are the timelines of FDA approvals of Olaparib across indications ^[1].

Approval Date	Approved Indication
March 11, 2022	FDA approved Lynparza® (Olaparib tablets) for the adjuvant treatment of adult patients with deleterious germline BRCA-mutated (gBRCAm) human epidermal growth factor receptor 2 (HER2)-negative high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy ^[2] .
May 20, 2020	Lynparza® (Olaparib tablets) was approved in the US for homologous recombination repair (HRR)- gene-mutated metastatic castration-resistant prostate cancer ^[1] .
May 8, 2020	FDA approved Lynparza® (Olaparib tablets) as a first-line maintenance treatment with bevacizumab for homologous recombination deficiency (HRD)-positive advanced ovarian cancer ^[1] .
December 30, 2019	Lynparza® (Olaparib tablets) was approved in the US as a first-line maintenance treatment of BRCA-mutated metastatic pancreatic cancer ^[1] .
December 19, 2018	Lynparza® (Olaparib tablets) was approved by US FDA for first-line maintenance therapy in BRCA-mutated advanced ovarian cancer ^[1] .
January 12, 2018	FDA approved Lynparza® (Olaparib tablets) for germline BRCA-mutated metastatic breast cancer ^[1] .
August 17, 2017	FDA approved Lynparza® (Olaparib tablets) for maintenance treatment of ovarian cancer ^[1] .
December 19, 2014	FDA approved Lynparza® (Olaparib tablets) to treat advanced ovarian cancer ^[1] .

Dr. Reddy's API Offering*

- We are among the earliest generic API manufacturers globally to file the USDMF for Olaparib API.
- In addition to the USDMF, considering the requirement of country-specific regulatory filings, we plan to diversify our drug master files (DMFs) with regulatory filling across various countries
- We offer Form-A (Innovator polymorph conducive for bioequivalence).

Specifications and Impurity Profile

S.No	Specifications	Result
1	API purity	SComprehensive impurity profile in accordance with ICH Q3A guidelines.
2	Genotoxic impurities	It is controlled below the threshold of toxicological concern (TTC).
3	Nitrosamine impurities	Based on our technical assessment of the synthetic route, the possibility of forming any of the N-nitroso dialkylamine impurities was avoided in our manufacturing process.
4	Storage conditions	Room Temperature (20 to 25 °C).
5	Particle size distribution (PSD)	<ul style="list-style-type: none">• Olaparib is a BCS Class IV drug, which requires a very fine PSD of the API to match the dissolution profile. We meet this requirement by offering a micronized API with customized particle sizes.• With the current process, PSD for "Form A" is D90 <50µm.• We are able to provide customized PSD to meet customer requirements.
6	Elemental impurities	Controlled elemental impurities below ICH Q3D permissible limit.
7	Retest period	Based on ongoing stability data, we have a 18 month re-test period, which will be extended based on future stability data points.

Manufacturing Capacity

- The current batch size of Olaparib is 15 kg. However, to meet the future global needs of Olaparib API, we are planning to ramp up the capacity to multi-tonnes by the financial year 2025.
- We manufacture Olaparib at our cGMP API manufacturing facilities (Table 3), successfully inspected by international regulatory authorities.

API Type	Manufacturing site	Current Batch Size
Olaparib (Crystalline form A)	CTO-SEZ (USFDA inspected, EuGMP certified site), API Srikakulam plant (SEZ) Sector No. 28 and 34, Devunipalavalasa village, Ranastalam Mandal, Srikakulam, Andhra Pradesh, India	15 kg

Supply Assurance

- Dr. Reddy's is well-positioned to meet the global demands for Olaparib API.
- We have reliable KSM suppliers to ensure timely deliveries and adherence to stringent specifications and multiple sources with sufficient capacity being added for key starting materials.
- We have reliable partners for all 3 KSMs and appropriate specifications designed for each KSM to meet API's desired critical quality attributes (CQAs).

Region Specific Suitability

- Our product is suitable for global formulation development.
- Our API (with four chemical conversions) is suitable for Brazil, China and Japan.

Proven Track Record in Drug Product Development

- We successfully commercialized Olaparib in multiple geographies and facilitated successful formulation development for our customers.
- As one of the earliest generic API manufacturers globally, we filed the USDMF for Olaparib API and can provide country-specific regulatory filings.

*Products under patent(s) are offered only for R&D purposes U/S 107A of the Patent Act and not for commercial sale.

For more information or to order sample quantities of APIs or formulations, log in to our customer service portal [XCEED](#) or contact us at api@drreddys.com.

References:

1. <https://www.drugs.com/history/lynpa.html>
2. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olaparib-adjuvant-treatment-high-risk-early-breast-cancer>

Disclaimer

The scientific content of this article has been developed by Dr. Reddy's Laboratories Limited ("DRL") for educational and awareness purpose only. Although greatest possible care has been taken in compiling, checking and developing the content to ensure that it is accurate and complete, Dr. Reddy's is not responsible or liable in the event of any damages or injury to any person in view of reliance placed or action taken basis of the information in this article. No part of the article including graphics available in this presentation may be copied or reproduced, in whole or in part, without the consent of Dr. Reddy's, other than for purposes permitted under fair use by copyright law. Products protected by valid patents are not offered for sale in countries where such products' sale constitutes patent infringement.