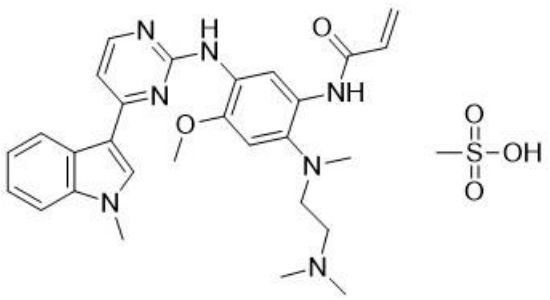
Product data sheet

MedKoo Cat#: 206426 Name: Osimertinib mesylate CAS#: 1421373-66-1 (mesylate) Chemical Formula: $C_{29}H_{37}N_7O_5S$ Molecular Weight: 595.72	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Osimertinib, also known as mereletinib and AZD-9291, is a third-generation EGFR inhibitor, showed promise in preclinical studies and provides hope for patients with advanced lung cancers that have become resistant to existing EGFR inhibitors. AZD9291 is highly active in preclinical models and is well tolerated in animal models. It inhibits both activating and resistant EGFR mutations while sparing the normal form of EGFR that is present in normal skin and gut cells, thereby reducing the side effects encountered with currently available medicines. Osimertinib was approved on Nov. 2015.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	10.0	16.78

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.68 mL	8.39 mL	16.79 mL
5 mM	0.34 mL	1.68 mL	3.36 mL
10 mM	0.17 mL	0.84 mL	1.68 mL
50 mM	0.03 mL	0.17 mL	0.34 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Takahashi A, Seike M, Chiba M, Takahashi S, Nakamichi S, Matsumoto M, Takeuchi S, Minegishi Y, Noro R, Kunugi S, Kubota K, Gemma A. Ankyrin Repeat Domain 1 Overexpression is Associated with Common Resistance to Afatinib and Osimertinib in EGFR-mutant Lung Cancer. Sci Rep. 2018 Oct 5;8(1):14896. doi: 10.1038/s41598-018-33190-8. PMID: 30291293; PMCID: PMC6173712.

2. Chagoya G, Kwatra SG, Nanni CW, Roberts CM, Phillips SM, Nullmeyergh S, Gilmore SP, Spasojevic I, Corcoran DL, Young CC, Ballman KV, Ramakrishna R, Cross DA, Markert JM, Lim M, Gilbert MR, Lesser GJ, Kwatra MM. Efficacy of osimertinib against EGFRvIII+ glioblastoma. Oncotarget. 2020 Jun 2;11(22):2074-2082. doi: 10.18632/oncotarget.27599. PMID: 32547705; PMCID: PMC7275784.

In vivo study

1. MacLeod AK, Lin D, Huang JT, McLaughlin LA, Henderson CJ, Wolf CR. Identification of Novel Pathways of Osimertinib Disposition and Potential Implications for the Outcome of Lung Cancer Therapy. Clin Cancer Res. 2018 May 1;24(9):2138-2147. doi: 10.1158/1078-0432.CCR-17-3555. Epub 2018 Feb 6. PMID: 29437786.

2. Floc'h N, Martin MJ, Riess JW, Orme JP, Staniszewska AD, Ménard L, Cuomo ME, O'Neill DJ, Ward RA, Finlay MRV, McKerrecher D, Cheng M, Vang DP, Burich RA, Keck JG, Gandara DR, Mack PC, Cross DAE. Antitumor Activity of Osimertinib, an Irreversible Mutant-Selective EGFR Tyrosine Kinase Inhibitor, in NSCLC Harboring EGFR Exon 20 Insertions. Mol Cancer Ther.

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2018 May;17(5):885-896. doi: 10.1158/1535-7163.MCT-17-0758. Epub 2018 Feb 26. PMID: 29483211; PMCID: PMC5932243.

7. Bioactivity

Biological target:

Osimertinib mesylate (AZD-9291 mesylate) is an irreversible and mutant selective EGFR inhibitor with IC50s of 12 and 1 nM against EGFRL858R and EGFRL858R/T790M, respectively.

In vitro activity

This study tried to construct a novel therapeutic strategy to conquer the resistance to second-and third-generation EGFR-TKIs in EGFR-positive NSCLC patients. Afatinib- and osimertinib-resistant lung adenocarcinoma cell lines were established. Exome sequencing, cDNA array and miRNA microarray were performed using the established cell lines to discover novel therapeutic targets associated with the resistance to second-and third-generation EGFR-TKIs. The third-generation EGFR-TKI, osimertinib, targets T790M and EGFR-activating mutations. MiRNA microarray analysis revealed miR-200a and miR-200b were remarkably downregulated in the osimertinib-resistant cell lines (Fig. 2a). Decreased expression of miR-200a, miR-200b and miR-200c were observed in the osimertinib-resistant cell lines by qRT-PCR CDNA microarray analysis was performed to identify the genes associated with resistance to afatinib and osimertinib using the parental and EGFR-TKIs-resistant NSCLC cells. ANKRD1 was the most and commonly upregulated gene in the four EGFR-TKIs-resistant cell lines. Long-term exposure of lung cancer cells to EGFR-TKIs may lead to accumulation of ANKRD1 protein. ANKRD1 inhibition or imatinib targeting ANKRD1 could rescue the acquired resistance to afatinib or osimertinib in EGFR-mutant cells. Recovery of the sensitivity to afatinib and osimertinib was also observed after imatinib treatment.

Reference: Sci Rep. 2018; 8: 14896. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6173712/

In vivo activity

To explore the influence of CYP1A enzymes on osimertinib disposition in vivo, this study carried out pharmacokinetic analysis in novel Cyp1a1/1a2 knockout and CYP1A1/1A2 humanized mouse lines. The basal expression of CYP1A1 in the h1A1/1A2 line is low, however it can be induced in a number of tissues including liver, lung, and small intestine by exposure of the mice to TCDD, an activator of the Ah receptor (Ahr). In h1A1/1A2 mice pretreated with TCDD, there was a 3.4-fold decrease in AUC0−t and a 3.3-fold decrease in Cmax of osimertinib (Fig. 5A and Supplementary Table S7). There was no change in exposure in the 1a1/1a2KO line. Correspondingly, TCDD-pretreatment greatly increased circulating levels of the OH-1 metabolite in humanized mice, but had no effect in knockouts (Fig. 5B). In this experiment, TCDD-mediated activation of Ahr occurred in several tissues—liver, small intestine, and lung—hence the effects on osimertinib and metabolite disposition were likely to be driven by a combination of hepatic, intestinal, and pulmonary CYP1A1/1A2.

Reference: Clin Cancer Res. 2018 May 1;24(9):2138-2147. https://clincancerres.aacrjournals.org/content/24/9/2138.long

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.