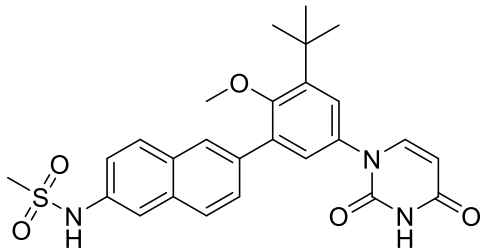
Product data sheet

MedKoo Cat#: 510275 Name: Dasabuvir (ABT-333) CAS#: 1132935-63-7 (free base) Chemical Formula: $C_{26}H_{27}N_3O_5S$ Exact Mass: 493.16714 Molecular Weight: 493.57468	
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:
Dasabuvir, also known as ABT-333, is a non-nucleoside polymerase inhibitor currently under clinical trials for the treatment of Hepatitis C. In the United States, it is approved by the Food and Drug Administration for use in combination with ombitasvir, paritaprevir, and ritonavir in the product Viekira Pak. Dasabuvir acts as a NS5B (an RNA-directed RNA polymerase) inhibitor.

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	55.0	111.43

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.03 mL	10.13 mL	20.26 mL
5 mM	0.41 mL	2.03 mL	4.05 mL
10 mM	0.20 mL	1.01 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 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. Kati W, Koev G, Irvin M, Beyer J, Liu Y, Krishnan P, Reisch T, Mondal R, Wagner R, Molla A, Maring C, Collins C. In vitro activity and resistance profile of dasabuvir, a nonnucleoside hepatitis C virus polymerase inhibitor. Antimicrob Agents Chemother. 2015 Mar;59(3):1505-11. doi: 10.1128/AAC.04619-14. Epub 2014 Dec 22. PMID: 25534735; PMCID: PMC4325770.
2. Stefanik M, Valdes JJ, Ezebuo FC, Haviernik J, Uzochukwu IC, Fojtikova M, Salat J, Eyer L, Ruzek D. FDA-Approved Drugs Efavirenz, Tipranavir, and Dasabuvir Inhibit Replication of Multiple Flaviviruses in Vero Cells. Microorganisms. 2020 Apr 20;8(4):599. doi: 10.3390/microorganisms8040599. PMID: 32326119; PMCID: PMC7232190.

In vivo study

1. Almomen A, Maher HM, Alzoman NZ, Shehata SM, Al-Taweel SM, Alanazi AA. Development and validation of UPLC-MS/MS method for studying the pharmacokinetic interaction of dasabuvir and tamoxifen, 4-hydroxytamoxifen in Wistar rats. Sci Rep. 2020 Feb 26;10(1):3521. doi: 10.1038/s41598-020-60613-2. PMID: 32103133; PMCID: PMC7044166.

7. Bioactivity
Biological target:

Dasabuvir (ABT-333) is a nonnucleoside inhibitor of the RNA-dependent RNA polymerase encoded by the HCV NS5B gene that inhibits recombinant NS5B polymerases derived from HCV genotype 1a and 1b clinical isolates, with IC50 between 2.2 and 10.7 nM.

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In vitro activity

Dasabuvir inhibited recombinant NS5B polymerases derived from HCV genotype 1a and 1b clinical isolates, with 50% inhibitory concentration (IC50) values between 2.2 and 10.7 nM, and was at least 7,000-fold selective for the inhibition of HCV genotype 1 polymerases over human/mammalian polymerases. In the HCV subgenomic replicon system, dasabuvir inhibited genotype 1a (strain H77) and 1b (strain Con1) replicons with 50% effective concentration (EC50) values of 7.7 and 1.8 nM, respectively, with a 13-fold decrease in inhibitory activity in the presence of 40% human plasma. This level of activity was retained against a panel of chimeric subgenomic replicons that contained HCV NS5B genes from 22 genotype 1 clinical isolates from treatment-naive patients, with EC50s ranging between 0.15 and 8.57 nM. Maintenance of replicon-containing cells in medium containing dasabuvir at concentrations 10-fold or 100-fold greater than the EC50 resulted in selection of resistant replicon clones. Consequently, dasabuvir retained full activity against replicons known to confer resistance to other polymerase inhibitors, including the S282T variant in the nucleoside binding site and the M423T, P495A, P495S, and V499A single variants in the thumb domain. Therefore, dasabuvir has the potential to play a key role in the treatment of HCV genotype 1 infections worldwide.

Reference: Antimicrob Agents Chemother. 2015 Mar;59(3):1505-11. https://pubmed.ncbi.nlm.nih.gov/25534735/

In vivo activity

The method was applied to investigate the PK interaction between DSV and TAM/TOH following the co-administration of DSV and TAM to Wistar rats. Moreover, DSV had no significant effect on the degree of TAM metabolism since no significant change ($p > 0.05$) in metabolite/parent ratio (M.R. %) was observed. Similarly, TAM/TOH has an inhibitory effect on CYP3A4 enzymes and P-gp transporters. Giving that DSV is metabolized mainly by CYP2C8 and to a lesser extent by CYP3A4 and that it is transported mainly by P-gp transporters, TAM was expected to increase DSV exposure through P-gp inhibition and CYP3A4 inhibition. Yet, the animal experiments revealed the absence of any significant effect of TAM on any of the measured PK parameters of DSV.

Reference: Sci Rep. 2020; 10: 3521. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7044166/