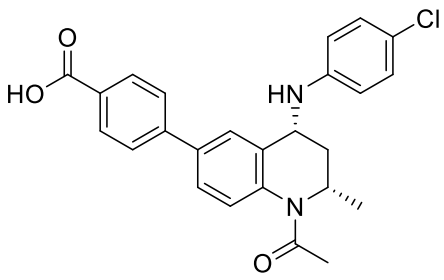
Product data sheet

MedKoo Cat#: 525336 Name: I-BET-726 CAS: 1300031-52-0 Chemical Formula: $C_{25}H_{23}ClN_2O_3$ Exact Mass: 434.1397 Molecular Weight: 434.92	
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:
I-BET-726, also known as GSK1324726A, is a potent and selective inhibitor of BET family proteins. Oral administration of I-BET726 to mouse xenograft models of human neuroblastoma results in tumor growth inhibition and down-regulation MYCN and BCL2 expression, suggesting a potential role for these genes in tumor growth.

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
DMF	30.0	68.98
DMSO	52.33	120.33
DMSO:PBS (pH 7.2) (1:4)	0.2	0.46
Ethanol	15.0	34.49

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.30 mL	11.50 mL	22.99 mL
5 mM	0.46 mL	2.30 mL	4.60 mL
10 mM	0.23 mL	1.15 mL	2.30 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Liu Z, Li P, Yang YQ, Cai S, Lin X, Chen MB, Guo H. I-BET726 suppresses human skin squamous cell carcinoma cell growth in vitro and in vivo. Cell Death Dis. 2020 May 5;11(5):318. doi: 10.1038/s41419-020-2515-z. PMID: 32371868; PMCID: PMC7200671.
2. Gosmini R, Nguyen VL, Toum J, Simon C, Brusq JM, Krysa G, Mirguet O, Riou-Eymard AM, Boursier EV, Trottet L, Bamborough P, Clark H, Chung CW, Cutler L, Demont EH, Kaur R, Lewis AJ, Schilling MB, Soden PE, Taylor S, Walker AL, Walker MD, Prinjha RK, Nicodème E. The discovery of I-BET726 (GSK1324726A), a potent tetrahydroquinoline ApoA1 up-regulator and selective BET bromodomain inhibitor. J Med Chem. 2014 Oct 9;57(19):8111-31. doi: 10.1021/jm5010539. Epub 2014 Sep 24. PMID: 25249180.

In vivo study

1. Liu Z, Li P, Yang YQ, Cai S, Lin X, Chen MB, Guo H. I-BET726 suppresses human skin squamous cell carcinoma cell growth in vitro and in vivo. Cell Death Dis. 2020 May 5;11(5):318. doi: 10.1038/s41419-020-2515-z. PMID: 32371868; PMCID: PMC7200671.

2. Wyce A, Ganji G, Smitheman KN, Chung CW, Korenchuk S, Bai Y, Barbash O, Le B, Craggs PD, McCabe MT, Kennedy-Wilson KM, Sanchez LV, Gosmini RL, Parr N, McHugh CF, Dhanak D, Prinjha RK, Auger KR, Tummino PJ. BET inhibition silences expression of MYCN and BCL2 and induces cytotoxicity in neuroblastoma tumor models. PLoS One. 2013 Aug 23;8(8):e72967. doi: 10.1371/journal.pone.0072967. PMID: 24009722; PMCID: PMC3751846.

7. Bioactivity

Biological target:

GSK1324726A is a novel, potent, and selective inhibitor of BET proteins with high affinity to BRD2 (IC_{50}=41 nM), BRD3 (IC_{50}=31 nM), and BRD4 (IC_{50}=22 nM).

In vitro activity

In A431 cells, I-BET726 (50 nm) was significantly more potent in inhibiting cell viability (Fig. S1A) and proliferation (Fig. S1B) than even higher concentrations of JQ1 (500 nm), CPI203 (500 nm), and AZD5153 (100 nm). These results show that I-BET726 potently inhibits survival, proliferation and migration of established and primary human skin SCC cells.

Reference: Cell Death Dis. 2020 May 5;11(5):318. https://pubmed.ncbi.nlm.nih.gov/32371868/

In vivo activity

In the CHP-212 model, treatment with 5 mg/kg I-BET726 resulted in TGI (tumor growth inhibition) equal to 50% (n=8; p= 0.1816; Figure 7C), and mice in the 15 mg/kg group exhibited a TGI of 82% at the end of the study (n=5; p =0.0488). Taken together, these data highlight the potential of BET inhibitors such as I-BET726 as potent anti-tumor agents in neuroblastoma, in part through the alteration of apoptotic and N-Myc-driven pathways.

Reference: PLoS One. 2013 Aug 23;8(8):e72967. https://pubmed.ncbi.nlm.nih.gov/24009722/