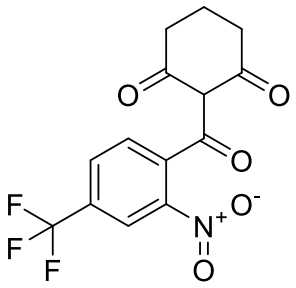
Product data sheet

MedKoo Cat#: 314265 Name: Nitisinone CAS#: 104206-65-7 Chemical Formula: $C_{14}H_{10}F_3NO_5$ Exact Mass: 329.05111 Molecular Weight: 329.23	
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:
Nitisinone, also known as NTBC, is an effective herbicide, is the licensed treatment for the human condition, hereditary tyrosinaemia type 1 (HT-1). Its mode of action interrupts tyrosine metabolism through inhibition of 4-hydroxyphenylpyruvate dioxygenase (HPPD). Nitisinone is a remarkable safe drug to use with few side effects reported.

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	30	91.1

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.04 mL	15.19 mL	30.37 mL
5 mM	0.61 mL	3.04 mL	6.07 mL
10 mM	0.30 mL	1.52 mL	3.04 mL
50 mM	0.06 mL	0.30 mL	0.61 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. Mistry JB, Jackson DJ, Bukhari M, Taylor AM. Osteoarticular cells tolerate short-term exposure to nitisinone-implications in alkaptonuria. Clin Rheumatol. 2016 Feb;35(2):513-6. doi: 10.1007/s10067-015-2983-1. Epub 2015 May 31. PMID: 26024586.

In vivo study

1. Onojafe IF, Megan LH, Melch MG, Aderemi JO, Alur RP, Abu-Asab MS, Chan CC, Bernardini IM, Albert JS, Cogliati T, Adams DR, Brooks BP. Minimal Efficacy of Nitisinone Treatment in a Novel Mouse Model of Oculocutaneous Albinism, Type 3. Invest Ophthalmol Vis Sci. 2018 Oct 1;59(12):4945-4952. doi: 10.1167/iovs.16-20293. PMID: 30347088; PMCID: PMC6181301.

2. Onojafe IF, Adams DR, Simeonov DR, Zhang J, Chan CC, Bernardini IM, Sergeev YV, Dolinska MB, Alur RP, Brilliant MH, Gahl WA, Brooks BP. Nitisinone improves eye and skin pigmentation defects in a mouse model of oculocutaneous albinism. J Clin Invest. 2011 Oct;121(10):3914-23. doi: 10.1172/JCI59372. PMID: 21968110; PMCID: PMC3223618.

7. Bioactivity
Biological target:
Nitisinone(SC0735) is an inhibitor of the enzyme 4-hydroxyphenylpyruvate dioxygenase.

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In vitro activity

Nitisinone's effect on chondrocytes and osteoblast-like cells was analyzed in an in vitro model. Human C20/A4 immortalized chondrocytes, and osteosarcoma cells MG63 cultured in DMEM, as previously described. Confluent cells were then plated into 24-well plates at 4 × 10(4) cells per well in varying concentrations of nitisinone. Cells were cultured for 7 days with medium changes every third day. Trypan blue assay was used to determine viability and the effect of nitisinone concentration on cells. Statistical analysis was performed using analysis of variance, and differences between groups were determined by Newman-Keuls post-test. Analysis of C20/A4 chondrocyte and MG63 osteoblast-like cell viability when cultured in different concentrations of nitisinone demonstrates that there is no statistically significant difference in cell viability compared to control cultures. There is currently no literature surrounding the use of nitisinone in human in vitro models, or its effect on chondrocytes or osteoblast like cells. These results show that nitisinone does not appear detrimental to cell viability of chondrocytes or osteoblast-like cells, which adds to the evidence that this therapy could be useful in treating AKU.

Reference: Clin Rheumatol. 2016 Feb;35(2):513-6. https://dx.doi.org/10.1007/s10067-015-2983-1

In vivo activity

Treatment with nitisinone increased tyrosine levels nearly 7-fold, resulting in an average concentration of 553 μM in the treated group compared with 80 μM in the control group, and much higher than the baseline tyrosine plasma content in other Tyr mutant mouse strains such as Tyrc-h/c-h (74–99 μM) and Tyrc-2J/c-2J (109–139 μM). Even though plasma tyrosine was substantially elevated, no discernible side effects were observed. The treated mice did not exhibit abnormal behavior or develop gross skin or corneal lesions, which can be side effects of hypertyrosinemia in humans. To quantify the effect of nitisinone on the number and size of melanosomes in ocular tissue, TEM of the iris, choroid, and RPE was performed (one eye each from n = 7 treated and n = 7 control mice) (Fig. 3). On processing of the images using ImageJ, and analysis of the data using two-tailed t-test, no statistically significant difference between the number of melanosomes in the RPE and choroid of treated compared with control mice was found (Fig. 4). However, it was detected that a statistically significant difference in the number of pigmented melanosomes in the iris stroma of the treated mice compared with untreated (Fig. 4). The cross-sectional area of melanosomes did not differ significantly between the two groups (Fig. 5). Melanosomes from all ocular tissues were between 0.048 and 0.8 μm2 in size and comparable to previously published melanosome size in choroid (0.07 ± 0.04 μm2) and RPE (0.12 ± 0.08 μm2) of wild-type C57BL/6J mice.40 These data demonstrate that treatment with nitisinone does not have a major impact on melanin pigmentation at either the gross or microscopic level in the C57BL/6J-Tyrp1b-J/b-J mouse model of OCA3.

Reference: Invest Ophthalmol Vis Sci. 2018 Oct 1;59(12):4945-4952. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30347088/