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产品名称：布喹那
产品别名：Brequinar；DUP785; NSC 368390

生物活性：

Description	Brequinar (DUP785) is a potent inhibitor of dihydroorotate dehydrogenase, with potent activities against a broad spectrum of viruses.
In Vitro	Brequinar reduces virus progeny production by >90%, with EC_{50} of 17 nM. Brequinar (5 μM) also inhibits other orthopoxviruses, and blocks virus DNA replication. Brequinar does not affect virus early gene expression, but has a severe effect on the late stage of the virus cycle[1]. Brequinar reduces the level of envelope protein production and the viral titer in a dose-dependent manner, with EC_{50} of 78 nM in the CFI assay. Brequinar (5 μM) inhibits viral RNA synthesis. Brequinar has antiviral effect, but the effect is reversed by pyrimidine. Brequinar-resistant viruses can be selected in cell culture. Brequinar (5 μM) suppresses the luciferase activities from both the WT and NS5 mutant replicons[2]. Brequinar sodium effectively prevents the increase in PyNTP levels with an IC_{50} of 0.26 μM. Brequinar sodium effectively inhibits cell proliferation with an IC_{50} of 0.26 μM. Brequinar sodium inhibits autophosphorylation of $p56^{lck}$ with IC_{50} of 70 μM; inhibition is 39, 41, and 60% for 25, 50, and 100 μM Brequinar sodium, respectively. Brequinar sodium also inhibits the phosphorylation by $p56^{lck}$ of the exogenous substrate, histone 2B, with an $IC_{50}$of 70 μM; inhibition is 10, 43, 59, and 86% for 25, 50, 100, and 200 μM Brequinar sodium, respectively. Brequinar sodium inhibits autophosphorylation of $p59^{fyn}$ with an IC_{50} of 105 μM; inhibition is 0, 17, 48, and 65% for 25, 50, 100, and 200 μM Brequinar sodium, respectively. Brequinar sodium also inhibits the phosphorylation by $p59^{fyn}$ of histone 2B with an IC_{50} of 20 μM; inhibition is 26, 54, 79, 83, and 84% for 10, 25, 50, 100, and 200 μM Brequinar sodium, respectively[3].
In Vivo	Brequinar sodium-treated (10-20 mg/kg/day) mice has a 31% reduction in percentage of packed cell volume compared with untreated BALB/c mice. Brequinar sodium reduces UTP and CTP levels in bone marrow cells by 30 and 25%, respectively. Brequinar sodium (10-20 mg/kg/day) in combination with uridine (1000-2000 mg/kg/day) prevents anemia, and the hematocrits remain at levels (61-63%) comparable with those of untreated controls[3].

In Vitro:

DMSO : 35.71 mg/mL (**95.13 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.6640 mL	13.3202 mL	26.6404 mL
	5 mM	0.5328 mL	2.6640 mL	5.3281 mL
	10 mM	0.2664 mL	1.3320 mL	2.6640 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储

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Solvent&Solubility	备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: 2.08 mg/mL (5.54 mM); Suspended solution; Need ultrasonic and warming 此方案可获得 2.08 mg/mL (5.54 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (5.54 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.54 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Schnellrath LC, et al. Potent antiviral activity of brequinar against the emerging Cantagalo virus in cell culture. Int J Antimicrob Agents. 2011 Nov;38(5):435-41. [2]. Qing M, et al. Characterization of dengue virus resistance to brequinar in cell culture. Antimicrob Agents Chemother. 2010 Sep;54(9):3686-95. [3]. Xu X, et al. In vitro and in vivo mechanisms of action of the antiproliferative and immunosuppressive agent, brequinar sodium. J Immunol. 1998 Jan 15;160(2):846-53.

实验参考：

Cell Assay	The neutral-red uptake assay is used to evaluate cell viability. BSC-40 cells are seeded in 96-well plates in the presence of concentrations of Brequinar ranging from 0.01 μM to 75 μM for 24 h. Control cells are incubated with 0.1% DMSO. Neutral red is methanol/acetic acid-extracted from cells and is quantitated at an absorbance of 490 nm (A490). All measurements expressed the average of four independent assays. [1]
Animal Administration	Brequinar is administered once daily by i.p. injection, while uridine is administered twice daily. Mice are bled through the orbital vein using a microhematocrit capillary tube, and the blood is centrifuged for 10 min at 550 × g. The percentage of packed cell volumes is determined with a microhematocrit capillary tube reader. All mice are killed 4 h after receiving their last dose of Brequinar or uridine. [3]
Kinase Assay	Immunoprecipitated $p59^{fyn}$ or $p56^{lck}$ from CTLL-4 cells or LSTRA cells (5×10^6) is preincubated with various concentrations of BQR in the PTK buffer (50 mM HEPES (pH 7.4), 10 mM $MgCl_2$, and 10 mM $MnCl_2$) on ice for 10 min. Exogenous substrate, histone 2B (2 μg), is added and, after 10 min, the reaction is initiated by addition of 10 μCi [γ-^{32}P]ATP. After incubation at 20°C for 10 min, the reaction mixture is subjected to electrophoresis in a 12.5% SDS-polyacrylamide gel. Phosphorylation of the kinase and the exogenous substrate is analyzed by autoradiography. [3]
References	[1]. Schnellrath LC, et al. Potent antiviral activity of brequinar against the emerging Cantagalo virus in cell culture. Int J Antimicrob Agents. 2011 Nov;38(5):435-41. [2]. Qing M, et al. Characterization of dengue virus resistance to brequinar in cell culture. Antimicrob

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