Dosing

Ravicti must be used with dietary protein restriction and sometimes with dietary supplements.

The daily dose should be individually adjusted according to the patient's protein tolerance and daily dietary protein intake. The recommended total daily dose of Ravicti is based on body surface area (BSA) and ranges from 4.5 ml/m²/day to 11.2 ml/m²/day.

The total daily dose should be divided into equal amounts and given with each meal or feeding (e.g. three to six times per day).

Each dose should be rounded up to the nearest 0.1 ml for patients less than 2 years of age and 0.5 ml for patients 2 years of age and older.

Recommended starting dose in phenylbuturate-naïve patients:

- **Body surface area (BSA) < 1.3 m²**
  8.5 ml/m²/day (9.4 g/m²/day)

- **Body surface area (BSA) ≥ 1.3 m²**
  7 ml/m²/day (8 g/m²/day)

Switching from all Sodium benzoate (NaBZ) formulations except injection to Ravicti

Patients switched from sodium benzoate should be considered as phenylbutyrate naïve and consequently should be dosed accordingly.

Initial dosage in patients switching from sodium phenylacetate/sodium benzoate injection to Ravicti

Once stable with controlled ammonia, patients switching to Ravicti should receive a dose of Ravicti at the higher end of the treatment (11 ml/m²/day) with measurements of plasma ammonia to guide further dosing.

References: 1. Ravicti SPC

Ravicti®▼ (glycerol phenylbutyrate) abbreviated prescribing information

For further prescribing information, please refer to the Ravicti Summary of Product Characteristics

Presentation: Each ml of liquid contains 1.1g of glycerol phenylbutyrate. **Indications:** Ravicti is indicated for use as adjunctive therapy for chronic management of patients with urea cycle disorders including deficiencies of carbamoyl phosphate synthetase I, ornithine carbamoyltransferase, argininosuccinate synthetase, argininosuccinate lyase, arginase I and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.
Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements. **Dosage and Administration**: Ravicti should be prescribed by a physician experienced in the management of UCDs. Ravicti liquid should be administered orally or via gastrostomy or nasogastric tube. The daily dose should be individually adjusted according to the patient's protein tolerance and the daily dietary protein intake needed. The recommended dosages for patients naïve to phenylbutyric acid and for patients switching from sodium phenylbutyrate or from sodium phenylacetate/sodium benzoate injection to Ravicti are different. The recommended total daily dose of Ravicti is based on body surface area and ranges from 4.5 ml/m2/day to 11.2 ml/m2/day [5.3 g/m2/day to 12.4 g/m2/day). Total daily dosage is given in equally divided dosages three to six daily. See SPC for full details. **Contraindications:** Hypersensitivity to the active substance and treatment of acute hyperammonaemia. **Warnings and Precautions:** Whilst on treatment with glycerol phenylbutyrate, acute hyperammonaemia including hyperammonaemic encephalopathy may occur in a proportion of patients. Ammonia levels should be monitored in patients with pancreatic insufficiency or intestinal malabsorption. High levels of the active metabolite PAA should be suspected in patients with unexplained somnolence, confusion, nausea and lethargy who have normal or low ammonia. **Overdose:** Phenylacetic acid is associated with signs and symptoms of neurotoxicity and could accumulate in patients who receive an overdose. **Pregnancy and Lactation**: Ravicti should not be used during pregnancy. **Undesirable Effects:** See SPC for full details. The most frequently reported adverse reactions during glycerol phenylbutyrate treatment were diarrhoea, flatulence, headache, decreased appetite, vomiting, fatigue, nausea and, skin odour abnormal. UK **List Price:** Ravicti 1.1 g/ml oral liquid. £161.00 per bottle excluding VAT. **EIRE List Price:** Available on request. **Legal Category:** POM. **Marketing Authorisation Numbers:** EU/1/15/1062/001. Further Information is available from Immedica Pharma UK Ltd, The Townhouse, 114-116 Fore Street, Hertford, Herts, SG14 1AJ. **Marketing Authorisation Holder:** Immedica Pharma AB, Norrtullsgatan 15, SE-113 29 Stockholm, Sweden **Date of Preparation:** February 2020 **Company Reference:** 001_RAV_UK_2020

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse reactions are to be reported according to national local regulations. Reporting forms and information can be found for UK at www.mhra.gov.uk/yellowcard and for Ireland at www.hpra.ie. Adverse reactions can also be reported to Immedica Pharma UK Ltd by email at safety@immedica.com

Immedica pharma

Immedica Pharma UK Ltd
The Townhouse
114-116 Fore Street
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SG14 1AJ

INFORMATION FOR HEALTHCARE PROFESSIONALS

Dosing and administration[1]

▼This medicine is subject to additional monitoring.
This will allow quickly identification of new safety information.

Immedica pharma

RAVICTI®▼
(glycerol phenylbutyrate) Oral Liquid
Rethink potential.

COM-000464, Date of Preparation: November 2020

Switch from NaPBA tablets

Total daily dosage of Ravicti (ml) = total daily dosage of sodium phenylbutyrate (NaPBA) tablets (g) x 0.86

Daily dose NaPBA (g)	Conversion from NaPBA tablets			Quantity of Ravicti bottles for 30 days therapy
	Equivalent total daily dose	Ravicti dose (daily dose divided 3)*	Rounded up the dose to the nearest 0.5 ml	
2	1.72	0.573	1	4
3	2.58	0.860	1	4
4	3.44	1.147	1.5	5
5	4.3	1.433	1.5	5
6	5.16	1.720	2	7
7	6.02	2.007	2.5	9
8	6.88	2.293	2.5	9
9	7.74	2.580	3	11
10	8.6	2.867	3	11
11	9.46	3.153	3.5	13
12	10.32	3.440	3.5	13
13	11.18	3.727	4	14
14	12.04	4.013	4.5	16
15	12.9	4.300	4.5	16
16	13.76	4.587	5	18
17	14.62	4.873	5	18
18	15.48	5.160	5.5	20
19	16.34	5.447	5.5	20
20	17.2	5.733	6	22

* Could be up to 6 times/day.

Switch from NaPBA granules (940 mg/g granules)

Total daily dosage of Ravicti (ml) = total daily dosage of sodium phenylbutyrate granules (g) x 0.81

Daily dose NaPBA (g)	Conversion from NaPBA granules**			Quantity of Ravicti bottles for 30 days therapy
	Equivalent total daily dose	Ravicti dose (daily dose divided 3)*	Rounded up the dose to the nearest 0.5 ml	
2	1.62	0.540	1	4
3	2.43	0.810	1	4
4	3.24	1.080	1.5	5
5	4.05	1.350	1.5	5
6	4.86	1.620	2	7
7	5.67	1.890	2	7
8	6.48	2.160	2.5	9
9	7.29	2.430	2.5	9
10	8.10	2.700	3	11
11	8.91	2.970	3	11
12	9.72	3.240	3.5	13
13	10.53	3.510	4	14
14	11.34	3.780	4	14
15	12.15	4.050	4.5	16
16	12.96	4.320	4.5	16
17	13.77	4.590	5	18
18	14.58	4.860	5	18
19	15.39	5.130	5.5	20
20	16.20	5.400	5.5	20

** For all other preparation of sodium phenylbutyrate, first calculate the total dose of NaPBA in g and x 0.86 to give a dose of Ravicti in ml.

Administration

Ravicti should be taken with meals and administered directly into the mouth via an oral syringe.

Ravicti may also be administered by a nasogastric or gastrostomy tube for those patients unable to take the product by mouth.

Pack contents

Each unit of Ravicti contains a glass bottle and a bottle adapter. It does not require any special storage conditions.