ABBREVIATED PRESCRIBING INFORMATION. The abbreviated prescribing information hereunder may vary in different countries. Before prescribing Rupafin 1 mg/ml oral solution please consult the full local approved Summary of Product Characteristics (SmPC).

Rupafin 1 mg/ml oral solution.

Name of the medicinal product: Rupafin 1 mg/ml oral solution**. Qualitative and quantitative composition:** Each ml of oral solution contains: 1 mg of rupatadine (as fumarate). Excipients with known effect: Sucrose 300 mg/ml**.** Methyl Parahydroxybenzoate (E218) 1.00 mg/ml. Propylene glycol (E-1520) 200 mg/ml**. Pharmaceutical form:** Oral solution. Clear yellow solution. **Therapeutic indications:** Rupafin 1 mg/ml oral solution is indicated for the symptomatic treatment of: -Allergic rhinitis (including persistent allergic rhinitis) in children aged 2 to 11 years. -Urticaria in children aged 2 to 11 years. **Posology and method of administration:** Children aged 2 to 11 years: *Dosage in children weighing equal or more than 25 kg*: 5 ml (5 mg of rupatadine) of oral solution once a day, with or without food. *Dosage in children weighing equal or more than 10 kg up to less than 25 kg*: 2.5 ml (2.5 mg of rupatadine) of oral solution once a day, with or without food. The administration of the product to children aged under 2 years is not recommended due to the lack of data in this population. In adults and adolescents (over 12 years of age), the administration of rupatadine 10 mg tablets is more appropriate. *Patients with renal or hepatic insufficiency:* As there is no clinical experience in patients with impaired kidney or liver functions, the use of rupatadine is at present not recommended in these patients. **Special warnings and precautions for use:** Safety of rupatadine oral solution in children aged less than 2 years has not been established. The combination of rupatadine with potent CYP3A4 inhibitors should be avoided and with moderate CYP3A4 inhibitors should be administered with caution. Dose adjustment of sensitive CYP3A4 substrates (e.g. simvastatin, lovastatin) and CYP3A4 substrates with a narrow therapeutic index (e.g. cyclosporin, tacrolimus, sirolimus, everolimus, cisapride) could be required as rupatadine may increase plasma concentrations of these drugs. The administration of rupatadine with grapefruit juice is not recommended. Cardiac safety of rupatadine 10 mg tablets was assessed in a Thorough QT/QTc study in adults. Rupatadine up to 10 times therapeutic dose did not produce any effect on the ECG and hence raises no cardiac safety concerns. However, rupatadine should be used with caution in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, patients with ongoing proarrhythmic conditions, such as clinically significant bradycardia, acute myocardial ischemia. Increases of blood creatine phosphokinase, alanine aminotransferase and aspartate aminotransferase, as well as abnormalities of liver function tests are uncommon adverse reaction reported with rupatadine 10 mg tablets in adults. This medicinal product contains sucrose, so it may be harmful to the teeth. Patients with rare hereditary problems of fructose intolerance, glucose/galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. This medicinal product contains methyl parahydroxybenzoate, may cause allergic reactions (possibly delayed). **Interaction with other medicinal products and other forms of interaction:** No interaction studies have been performed in children with rupatadine oral solution. Interaction studies have only been performed in adults and adolescents (over 12 years of age) with rupatadine 10 mg tablets. *Effects of other drugs on rupatadine:* Co-administration with potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV protease inhibitors, clarithromycin, nefazodone) should be avoided and co-medication with moderate CYP3A4 inhibitors (erythromycin, fluconazole, diltiazem) should be used with caution. The concomitant administration of rupatadine 20 mg and ketoconazole or erythromycin increases the systemic exposure to rupatadine 10 times and 2-3 times respectively. These modifications were not associated with an effect on the QT interval or with an increase of the adverse reactions in comparison with the drugs when administered separately. Interaction with grapefruit: The concomitant administration of grapefruit juice increased 3.5 times the systemic exposure of rupatadine 10 mg tablet. This occurs because grapefruit has one or more compounds that inhibit

the CYP3A4 and can increase the plasmatic concentrations of drugs metabolised through this CYP3A4, like rupatadine. In addition, it has been suggested that the grapefruit can affect intestinal drug transport systems as the glycoprotein-P. Grapefruit juice should not be taken simultaneously. *Effects of rupatadine on other drugs:* Caution should be taken when rupatadine is co-administered with other metabolised drugs with narrow therapeutic windows since knowledge of the effect of rupatadine on other drugs is limited. Interaction with alcohol: After administration of alcohol, a dose of rupatadine 10 mg tablet produced marginal effects in some psychomotor performance tests although they were not significantly different from those induced by intake of alcohol only. A dose of 20 mg increased the impairment caused by the intake of alcohol. Interaction with CNS depressants: As with other antihistamines, interactions with CNS depressants cannot be excluded. Interaction with statins: Asymptomatic CPK increases have been uncommonly reported in rupatadine clinical trials. The risk of interactions with statins, some of which are also metabolised by the cytochrome P450 CYP3A4 isozyme, is unknown. For these reasons, rupatadine should be used with caution when it is co-administered with statins. Interaction with midazolam: After the administration of 10 mg rupatadine in combination with 7.5 mg midazolam, an increase of exposure (Cmax and AUC) of midazolam was mildly higher observed. For this reason, rupatadine acts as a mild inhibitor of CYP3A4. **Effects on the ability to drive and use machines:** Rupatadine 10 mg had no influence on the ability to drive and use machines in a performed clinical trial. Nevertheless, care should be taken before driving or using machinery until the patient's individual reaction to rupatadine has been established. **Fertility, pregnancy and lactation:** Pregnancy: Data on a limited number (2) of exposed pregnancies indicate no adverse effects of rupatadine on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. As a precautionary measure, it is preferable to avoid the use of rupatadine during pregnancy. Breastfeeding: Rupatadine is excreted in animal milk. It is unknown whether rupatadine is excreted into breast milk. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from rupatadine therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. Fertility:There are no clinical data on fertility. Studies in animals have shown a significant reduction of fertility at exposure levels higher than those observed in humans at the maximum therapeutic dose. **Undesirable effects:** Clinical trials with rupatadine oral solution in children aged 2-11 years included 626 patients. From these, 147 patients were treated with rupatadine 2.5 mg, 159 patients were treated with rupatadine 5 mg, 249 received placebo and 71 received desloratadine. The frequencies of adverse reactions reported in patients treated with rupatadine oral solution during clinical trials were as follows:

System Organ Class term Frequency	*Preferred term*	Rupatadine 2.5 mg (n=147)	Rupatadine 5 mg (n=159)	Placebo (n=249)
	Infections and infestations			
Uncommon	*Influenza*	0	1 (0.63%)	0
	Nasopharyngitis	1 (0.68%)	0	0
	Upper respiratory tract infection	1 (0.68%)	0	0
	Blood and lymphatic system disorders			
Uncommon	*Eosinophilia*	0	1 (0.63%)	0

System Organ Class term Frequency	*Preferred term*	Rupatadine 2.5 mg (n=147)	Rupatadine 5 mg (n=159)	Placebo (n=249)
	Neutropenia	0	1 (0.63%)	0
	Nervous system disorders			
Common	*Headache*	2 (1.36%)	4 (2.52%)	4 (1.61%)
	Somnolence	0	2 (1.26%)	0
Uncommon	*Dizziness*	0	1 (0.63%)	1 (0.40%)
	Gastrointestinal disorders			
Uncommon	*Nausea*	0	1 (0.63%)	2 (0.80%)
	Skin and subcutaneous tissue disorders			
Uncommon	*Eczema*	0	1 (0.63%)	1 (0.40%)
	Night sweats	0	1 (0.63%)	0
	General disorders and administration site conditions			
Uncommon	*Fatigue*	0	1 (0.63%)	0

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. **Marketing authorisation holder:** Noucor Health, S.A., Av. Camí Reial, 51-57, 08184 Palau-solità i Plegamans (Spain).

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For further information please contact our local representative or Noucor: Av. Camí Reial, 51-57, 08184 Palau-solità i Plegamans (Spain). Phone +34 93 737 66 90.