SUMMARY OF PRODUCT CHARACTERISTICS
(as authorized in the Czech Republic)

1. NAME OF THE MEDICINAL PRODUCT

IMUNOR

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Transferendi factor suillus 10 mg in each vial

The active substance is a soluble ultra-filtered extract prepared using peripheral porcine blood leukocytes (transfer factor). Drinking water should be used as a solvent.

3. PHARMACEUTICAL FORM

Oral lyophilizate

Product description: Porous, white to off-white mass in the form of a cake or a dispersed powder. The powder can get adhered to the bottom or a stopper of the vial.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The active substance is a mixture of low-molecular peptides and nucleoprotein grafts with a low molecular mass (less than 12 000 D), including regulative products of T lymphocytes that are released, under physiological conditions, by immunocompetent cells during an immune response. The proportional composition of the low-molecular substance mixture is characterized by the absorbency ratio at 260 and 280 nm.
A260
------- higher or equal to 1.8
A280

IMUNOR is indicated for the treatment primarily in cases of a laboratory confirmed cellular immunity disorder (a decrease of the total T lymphocyte count, deviations from the number of CD4+ and CD8+ T lymphocyte subpopulations); furthermore, it is indicated in clinical cases of diseases known to be usually associated with impairment of cellular immunity. IMUNOR is also indicated to treat humoral immunity deficiencies with laboratory confirmed reduced levels of immunoglobulins and irregular findings of affected cellular immunity with a clinical picture of recurring infections of various locations.

The following types of disease are especially concerned: Primary immunodeficiency: For instance, a common variable immune deficiency, particularly with manifestations of chronic and/or recurrent bacterial infections and a proof of impaired cellular immunity functions. Secondary immunodeficiency: Adjuvant therapy at the protracted recovery after some viral diseases; conditions after complicated surgical interventions performed under general anesthesia with symptoms of reduced immunocompetence; adjuvant therapy of malignant diseases at the phase after chemotherapy and radiotherapy with the symptomatology of the

lowered immunity functions (recurring infections, sub-febrile conditions, fatigue, leucopenia); recovery after septic conditions; chronic and recurrent infections with a difficult response to current therapy; chronic fatigue syndrome – cases exhibiting reduced cell-immunity parameters; recurrent herpetic diseases (herpes simplex, herpes genitalis). IMUNOR has also produced good results in the treatment of some allergic diseases (asthma bronchiale) as a complementary therapy to the standard treatment (antihistaminic agents, prophylactic immunopharmaceuticals), or to the subsequent immunotherapy (auto-vaccines, hypo-sensitization). It is also used with good results at the treatment of superficial mycoses.

IMMUNOR is indicated for the treatment of adults and children from 3 years of age.

4.2 Posology and method of administration

Dosage
There is no difference in dosage for individual age categories.
The basic cure (the basic therapeutic treatment) consists in administration of four to six doses of the product at one-week intervals. In a case of an acute infection, the treatment can be also commenced via administration of two to three doses during the first week (e.g. every other day), with the subsequent administration of further doses at one-week intervals. The selection of the therapeutic strategy is individualized and depends on the clinical development of the case and on laboratory findings in terms of immunology. As a rule, three to four therapeutic treatments are repeated in a year. In more serious cases - when the disease recurs frequently during periods between individual therapeutic treatments - the product can be administered continuously. This usually means a long-term administration of one dose at one-week or two-week intervals.

Route of administration
After reconstitution, the product should be drunk in the morning on an empty stomach; and after half an hour, a light breakfast can be eaten.

Instructions for reconstitution of this medicinal product prior to its use can be found in section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance.
Pregnancy.

4.4 Special warnings and precautions for use

No serious adverse drug reactions have been reported so far.

The product can be administered to patients with renal insufficiency.
IMUNOR treatment should be conducted under supervision of a clinical immunologist.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions studies have been carried out.

4.6 Fertility, pregnancy and lactation

Pregnancy
Pregnancy is a contraindication for IMUNOR administration.

Lactation
Efficacy and tolerance of the product have not been verified in breast-feeding women so far.

4.7 Effects on ability to drive and use machines

IMUNOR has no or a negligible influence on the ability to drive or operate machines.

4.8 Undesirable effects

IMUNOR tolerance is generally very good. The following adverse drug reactions have been reported in sporadic cases:
Gastrointestinal disorders: Manifestations of mild gastrointestinal intolerance (nausea, burning in epigastrium, vomiting);
Skin and subcutaneous tissue disorders: Itching, transient exanthema;
General disorders and administration site conditions: Fatigue, somnolence, higher sweating, headaches, feeling of internal warm.

The adverse drug reactions are mostly of a transient character and they have led to a necessity of discontinuance of the treatment in exceptional cases only.

No serious adverse drug reactions have been reported.

Reporting of suspected adverse reactions
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 at the below address:

Státní ústav pro kontrolu léčiv
Šrobárova 48
100 41 Praha 10
Web sites: www.sukl.cz/nahlasit-nezadouci-ucinek

4.9 Overdose

In view of the results of preclinical testing, the overdose has not been studied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunostimulants, ATC code: L03AX

Mode of action
The mode of action of IMUNOR (transfer factor) is complex. The transfer effect on its own results in activation of non-competent lymphocytes and, thus, they are able to identify foreign antigens and react to them by proliferation and differentiation. At the same time, numerous non-specific alterations take place after IMUNOR administration.

Pharmacodynamic effects
The pharmacodynamic effects consist in activation of chemotaxis, the phagocyte activity of macrophages and polymorphonuclears, in an induction of the interferon and interleukin creation, in normalization of a number of total T lymphocytes and PHA-reacting lymphocytes, in activation of cyclic nucleotides (cGMT), in normalization of the blood picture constituents, in higher synthesis of nucleic acids, and in anti-inflammatory and anti-edematous effects. The above mentioned activities do not result in exceeding the normal-value parameters. Hence, IMUNOR seems to be a substance modulating the entire immune system; and in preclinical testing, the effect of IMUNOR did not differ markedly from the standard human transfer factor administered subcutaneously.

Clinical safety and efficacy
Based on results of clinical testing, it may be stated that IMUNOR administration resulted in an adjustment of both reduced and increased values of studied parameters (being outside the given physiological range) as ascertained at the start of the study. The values were modified during the study towards their physiological range. That is why a lower percentage of persons with out-of-limit values were recorded at the end of the study in majority of cases. IMUNOR administration has demonstrated a favorable influence on fatigue as well as sub-febrile temperatures going away, or a beneficial impact on the frequency and severity of course of infections. In vast majority of patients, the health state got improved thanks to IMUNOR.

The product tolerance was very good. Only three out of 135 patients had to be excluded from the study owing to adverse drug reactions of higher intensity.

5.2 Pharmacokinetic properties

The pharmacokinetic study was not carried out for technical reasons. The product is a soluble ultra-filtered extract prepared of porcine peripheral blood leukocytes. The active substance is a mixture of low-molecular peptides and nucleoprotein grafts of low molecular mass (lower than 12 000 D), incl. regulative products of T lymphocytes released under physiological conditions by immunocompetent cells at an immune response. This mixture of substances could not be differentiated from substances proper to the organism using available methods.

5.3 Preclinical safety data

No particular risk for humans has been revealed based on non-clinical data obtained from conventional studies of pharmacological safety, multiple dosage toxicity, genotoxicity, carcinogenicity, or reproduction and development toxicity studies.

At preclinical testing of the transfer factor by the VÚFB (the Research Institute of Pharmacy and Biochemistry), safety of the factor was studied in a seven-day tolerance study on mice and rats. Furthermore, a special test was carried out investigating potential embryotoxicity of the product tested.

IMUNOR is very well tolerated. The seven-day administration of the product to mice and rats, dosed daily 0.15 mg/kg and 7.5 mg/kg orally (i.e. an equivalent and in a fifty-fold multiple of the supposed clinical dose), did not induce any alteration indicating the product toxic influence on clinical, hematological or biochemical parameters studied. Neither pathological/anatomical, nor histological, nor ultra-structural examination indicated toxic effects of IMUNOR.

No alterations indicating embryo-toxic activity of IMUNOR in the CHEST I and II test on a chicken embryo were confirmed. Neither mutagenic activity was ascertained.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

No compatibility studies are available. Therefore, this medicinal product must not be mingled with other medicinal products.

6.3 Shelf-life

In an intact package, the shelf-life is 18 months. After reconstitution according to instructions, the product must be consumed immediately.

6.4 Special precautions for storage

Store in a fridge at 2 - 8 ^{0}C; the vials should be kept in their box to protect the product from light.
Do not use after expiry of the shelf-life given on the package.
Keep out of sight and reach of children.

6.5 Nature and contents of container

A glass vial of 3 ml in each, closed with a lyophilization stopper and a plastic screw cap. The vials are packed 4 pieces in each paper folding box.

6.6 Special precautions for handling and disposal

Reconstitute the contents of the vial before administration by adding drinking water up to the neck of the vial and moderately shake. Since the powder can get adhered to the stopper, it is advisable to close the vial again after water addition and to shake it in order to achieve a perfect reconstitution of the powder in the water. Then drink the contents on an empty stomach; a light breakfast can be taken after half an hour thereafter.

The unused medicinal product or its wastes must be disposed of in compliance with requirements of local legislation.

7. MARKETING AUTHORISATION HOLDER

ImunomedicA a.s., Chuderov 118, 400 02 Ústí n. Labem, Czech Republic

8. MARKETING AUTHORISATION NUMBER(S)

59/516/97-C

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 25.6.1997
Date of renewal of the authorization: 25.6.2014

10. DATE OF REVISION OF THE TEXT

19.5.2015