APPROVED PROFESSIONAL INFORMATION FOR OCTANORM®

SCHEDULING STATUS S4

1. NAME OF MEDICINE

OCTANORM® solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

OCTANORM is a solution of human immunoglobulin G fraction from pooled human blood.

OCTANORM contains per 1 ml solution:

Human immunoglobulin - 165 mg (corresponding to human protein content of which at least 95 % is IgG).

Distribution of IgG subclasses:

IgG1 59 %

IgG2 36 %

IgG3 4,9 %

IgG4 0,5 %

IgA maximum 82,5 µg/ml

OCTANORM contains no antimicrobial agents or preservatives.

The pH of the solution is between 6,4 and 7,2.

Excipient(s) with known effect:

OCTANORM contains 4,35 mmol (or 100 mg) sodium per dose (40 ml)

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

OCTANORM is clear or slightly opalescent and colourless or pale-yellow or light brown solution.

Free of visible particles

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

OCTANORM is indicated for replacement therapy in adults and children with primary immuno-deficiency syndromes such as:

- congenital agammaglobulinaemia and hypogamma-globulinaemia,
- common variable immunodeficiency (CVID),
- severe combined immunodeficiency,
- lgG subclass deficiencies with recurrent infections.

4.2 Posology and method of administration

Posology

Replacement therapy

The treatment should be initiated and monitored under the supervision of a medical practitioner experienced in the treatment of immunodeficiency.

The dosage may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dosage regimens are given as guidance.

Subcutaneous injection

The dosage regimen using the subcutaneous route should achieve a sustained level of lgG.

A loading dose of at least 0,2 - 0,5 g/kg may be required.

After steady state lgG levels have been attained, maintenance doses are administered at repeated intervals to reach a cumulative monthly dose of the order of 0,4 - 0,8 g/kg.

If loading dose is given divided in daily doses over 3 - 5 days, steady state is achieved within one week.

If treatment is done by giving weekly doses from beginning, steady state is achieved within 6 months.

Trough levels should be measured in order to adjust the dose and dosage interval.

Paediatric population

Data on children suffering from PID are available. As with adults, trough levels should be measured in order to adjust the dose and dosage interval. After steady state lgG levels have been attained, maintenance doses of about 80 to 100 mg/kg/week are usually administered to reach a cumulative monthly dose of the order of 0,4 - 0,8 g/kg.

If home treatment is considered, advice from a physician experienced in the guidance of patients for home treatment should be sought. The patient's parents should be instructed in the use of the application device, infusion techniques, the keeping of a treatment diary and measures to be taken in case of severe adverse events.

Method of administration

OCTANORM should be administered via the subcutaneous route.

Subcutaneous infusion for home treatment should be initiated by a medical practitioner experienced in the guidance of patients for home treatment. The patient will be instructed in the use of a syringe driver, infusion techniques, the keeping of a treatment diary and measures to be taken in case of severe adverse events.

Subcutaneous infusion with pump

The usual dose is 0,6 ml (100 mg) **OCTANORM** per kg bodyweight once a week, which should be administered at different infusion sites. Initial infusion rate: 10 ml/hour/pump. The infusion rate may be gradually increased by 1 ml/hour/pump every three to four weeks. The maximum dose

administered has been 40 ml/hour using two pumps simultaneously. When large doses are given, it is advisable to administer them in divided doses at different sites.

4.3 Contraindications

- **OCTANORM** is contraindicated in patients with hypersensitivity to immunoglobulin containing preparations including **OCTANORM** or to any other ingredients in **OCTANORM** (see section 6.1.)
- **OCTANORM** must not be given intravenously.
- **OCTANORM** must not be administered intramuscularly in cases of severe thrombocytopenia and in other disorders of haemostasis.

4.4 Special warnings and precautions for use

In the absence of compatibility studies, **OCTANORM** must not be mixed with other medicinal products.

If **OCTANORM** is accidentally administered into a blood vessel, patients could develop anaphylactic shock.

The recommended injection rate (see section 4.2 "**Method of administration**") should be adhered to.

OCTANORM does not protect against hepatitis A.

Patients should be closely monitored and carefully observed for any adverse events throughout the injection period and for at least 20 minutes after the injection.

Certain adverse reactions may occur more frequently in patients who receive **OCTANORM** for the first time or, when a human normal immunoglobulin product is switched or when treatment has been stopped for more than eight weeks. True hypersensitivity reactions are rare.

They can particularly occur in the case of lgA deficiency with anti-lgA antibodies and these patients should be treated with caution.

OCTANORM can induce a fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with human immunoglobulin.

Potential complications can often be avoided by ensuring that:

- patients are not sensitive to human immunoglobulin, by first injecting the product slowly (See section 4.2 "**Method of administration"**).
- patients are carefully monitored for any symptoms throughout the injection period.
- In particular patients
    - naïve to human immunoglobulin
    - switched from an alternative product
    - when there has been a long interval since the previous injection should be monitored during the first injection and for the first hour after the first injection, in order to detect potential adverse signs.

All other patients should be observed for at least 20 minutes after administration. If allergic or anaphylactic-type reactions occur, the injection should be stopped immediately and appropriate treatment instituted. In case of shock, the current medical standards for shock treatment should be implemented.

Thromboembolism

Arterial and venous thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism have been associated with the use of immunoglobulins. Caution should be exercised in patients with pre-existing risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilisation, severely hypovolaemic patients, patients with diseases which increase blood viscosity).
Patients should be informed about first symptoms of thromboembolic events including shortness of breath, pain and swelling of a limb, focal neurological deficits and chest pain and should be advised to contact their medical practitioner immediately upon onset of symptoms. Patients should be sufficiently hydrated before use of **OCTANORM.**

The measures to prevent infections of blood borne disease may be of limited value against non-enveloped viruses such as HAV and parvovirus B19.

It is strongly recommended that, every time that **OCTANORM** is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

OCTANORM contains 4,35 mmol (or 100 mg) sodium per dose (40 ml) and should be taken into consideration by patients on a low sodium diet.

4.5 Interactions with other medicines and other forms of interaction

Live attenuated virus vaccines

OCTANORM administration may impair the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella, for a period of at least 6 weeks and up to 3 months.

After administration of **OCTANORM** an interval of 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 1 year. Therefore, patients receiving measles vaccine should have their antibody status checked.

Interference with serological testing

After injection of **OCTANORM** the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing. Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D may interfere with some serological tests (reticulocyte count, haptoglobin and antiglobulin test).

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of **OCTANORM** for use in pregnancy has not been established.

Lactation

OCTANORM excreted into the breast milk. **OCTANORM** should therefore only be given with caution to pregnant women and breastfeeding mothers.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

a. Summary of the safety profile

Adverse reactions for **OCTANORM** are rare

In case of severe reactions, the injection should be stopped, and an appropriate treatment should be initiated.

b. Tabulated list of adverse reactions

The following adverse reactions have been observed for **OCTANORM** during the post-marketing phase:

Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (<1/10 000). Including isolated reports

MeDRA System Organ class (SOC)	Adverse Reaction and Frequency		
	Common	Rare	Very Rare
Immune system		hypersensitivity	anaphylactic shock
Nervous system disorder			headache, dizziness
Vascular disorder		hypotension	thromboembolic events
Gastrointestinal disorders			nausea, vomiting
Musculoskeletal, connective tissue and bone disorders			back pain, arthralgia
General disorders and administrative site conditions	Injection site reaction		Fever, rigors, fatique

c. Paediatric population

For the paediatric population no specific adverse reactions are expected.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Adverse drug reaction and product quality reporting form, found online under SAHPRA's E-Services: https://www.sahpra.org.za/ e-Library/GLF-CEM PV-06A.

4.9 Overdose

Consequences of an overdose are not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 30.1 Biologicals (Antibodies)

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for extravascular administration, ATC code: J06BA01

Human immunoglobulin contains mainly immunoglobulin G (lgG) which is antibodies against infectious agents. It is prepared from pooled plasma and has a distribution of immunoglobulin G subclasses closely proportional to that in natural human plasma.

5.2 Pharmacokinetic properties

The bioavailability is close to 100 %. With subcutaneous administration of human immunoglobulin, peak levels are achieved in the recipient's circulation after a delay of 4 – 6 days.

Data from clinical studies show that trough levels of lgG can be maintained by dosing regimens of 100 mg/kg per week.

With intramuscular administration, lgG peak levels in the recipient's circulation is achieved after a delay of 2 – 3 days.

lgG and lgG-complexes are broken down in the cells of the reticulo-endothelial system.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine, polysorbate 80, sodium chloride, sodium acetate and water for injections.

6.2 Incompatibilities

In the absence of compatibility studies, **OCTANORM** must not be mixed with other medicinal products.

6.3 Shelf-life

3 years.

Within its shelf-life, the unopened vial may be stored at or below 25 ºC for up to 6 months, without being refrigerated again during this period, and must be discarded if not used after the storage at or below 25 ºC for the six months period.

6.4 Special precautions for storage

Store and transport between 2 °C to 8 °C and DO NOT FREEZE.

Protect from light by storing in the original carton (secondary container).

6.5 Nature and contents of containers

6 ml and 12 ml of solution filled in a 20 ml clear glass vial (type I) with a bromobutyl rubber stopper with a flip-off cap.

Pack of 1, 10 or 20.

24 ml or 48 ml of solution in a 50 ml clear glass vial (type I) with a bromobutyl rubber stopper with a flip-off cap.

Pack of 1, 10 or 20.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

OCTANORM should be brought to room or body temperature before use.

The solution should be clear or slightly opalescent and colourless or pale yellow or light brown. Do not use solutions that are cloudy or have deposits.

Once the vial has been opened the content should be used immediately.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

OCTAPHARMA SA (Pty) Ltd.
Building # 3, Design Quarter complex
Cnr Winnie Mandela Drive and Leslie Ave East
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8. REGISTRATION NUMBER

51/30.1/0731

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 June 2020

10. DATE OF REVISION OF THE TEXT

15 September 2025