Public Assessment Report

UKPAR

Aragam 50 mg/ml solution for infusion
(human normal immunoglobulin)

UK Licence No: PL 21838/0003

Oxbridge Pharma Limited
LAY SUMMARY
Aragam 50 mg/ml solution for infusion
(human normal immunoglobulin)

This is a summary of the Public Assessment Report (PAR) for Aragam 50 mg/ml solution for infusion (PL 21838/0003). It explains how Aragam 50 mg/ml solution for infusion was assessed and its authorisation recommended as well as its conditions of use. It is not intended to provide practical advice on how to use this product. This report will refer to Aragam 50 mg/ml solution for infusion, as Aragam from this instance onward.

For practical information about using Aragam, patients should read the package leaflet or contact their doctor or pharmacist.

What is Aragam and what is it used for?
Aragam is a prescription-only medicine (legal status POM) containing the active ingredient human normal immunoglobulin. Immunoglobulins are antibodies and normal constituents of human blood, and they help to protect against infections.

How does Aragam work?
Aragam is used to raise antibody levels in the blood when the antibody level is too low, or if you need additional antibodies in certain diseases. The administration of antibodies can also have an effect in case of a disrupted immune system.

How is Aragam used?
Aragam can only be obtained with a prescription

Aragam is usually administered by a doctor or nurse. It may also be self-administered if this is an approved practice in the prescribing country and only when the patient is has been trained sufficiently.

Aragam is intended for infusion into a vein. The dosage will vary depending on the condition being treated and the bodyweight of the patient. The doctor will provide guidance about the dosage and infusion rate to patients self-administering Aragam.

Please read Section 3 of the patient information leaflet for detailed information on dosing recommendations, the route of administration and the duration of treatment.

What benefits of Aragam have been shown in studies?
Clinical studies were submitted with this application to show that it is effective in raising antibody levels in the blood. The non-clinical and clinical data submitted are identical to those submitted for the grant of another product licence, Nanogram 50mg/ml solution for infusion (PL 16935/0004).

What are the possible side effects of Aragam?
The possible side effects observed with Aragam are the same as those observed with the duplicate product.

For further information, please see the ‘Possible Side Effects’ section of the patient information leaflet.

Why was Aragam approved?
It was concluded that, in accordance with EU requirements that the pharmaceutical, non-clinical and clinical data submitted for Aragam is the same as that submitted for Nanogam 50 mg/ml solution for infusion (PL 16935/0004). Therefore, the MHRA decided that, as for Nanogam 50 mg/ml solution for infusion (PL 16935/0004), the benefits outweigh the identified risks and recommended that Aragam can be approved for use.
What measures are being taken to ensure the safe and effective use of Aragam?
Suitable measures have been put in place to monitor the use of this product, including the recording and submission of any adverse effects to the relevant authorities in a timely manner. Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Aragam
A Marketing Authorisation was granted in the UK on 22 September 2011.

The full PAR for Aragam follows this summary. For more information about treatment with Aragam read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in October 2016.
# SCIENTIFIC DISCUSSION

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Aragam (PL 21838/0003) could be approved.

This application was submitted as a standard abridged national application, including all modules, in accordance with Article 8(3), known active substance, of Directive 2001/83/EC. The pharmaceutical, non-clinical and clinical data submitted is the same as for Nanogam 50 mg/ml solution for infusion (PL 16935/0004) granted to Stichting Sanquin Bloedvoorziening following an incoming mutual recognition repeat-use procedure, F1/H/357/01/E/002. Any differences in wording in the patient information reflect comments from the MHRA during the previous assessment and implementation of the core SmPC for human normal immunoglobulin for intravenous administration. A statement of the level of IgA is also required by the European Pharmacopoeia.

Aragam is a prescription-only medicine (legal classification POM). This product contains the active substance human normal immunoglobulin. Immunoglobulins are antibodies and normal constituents of human blood.

This product is indicated for the treatment of following:

Replacement therapy (treatment of patients who do not have sufficient antibodies) in adults, and children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes (diseases which are caused by a hereditary disorder of the immune system) with impaired antibody production.
- Hypogammaglobulinemia (complete or partial lack of the immune response caused by a complete or partial deficit of antibodies) and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (malignant bleeding disorder), in whom prophylactic antibiotics have failed.
- Hypogammaglobulinemia and recurrent bacterial infections in plateau phase multiple myeloma (malignant bone marrow tumour) patients who have failed to respond to pneumococcal immunisation.
- Hypogammaglobulinemia in patients after allogenic haematopoietic stem cell transplantation (HSCT).
- Congenital AIDS with recurrent bacterial infections.

Immunomodulation (influencing a disrupted immune system) in adults, and children and adolescents (0-18 years) in:

- Primary immune thrombocytopenia (ITP, a bleeding disorder caused by a reduced number of platelets), in patients at risk of bleeding or prior to surgery to correct the platelet count.
- Guillain Barré syndrome (this is a syndrome of unknown cause at which muscle paralysis occur).
- Kawasaki disease (a very rare disease in children with defects of the skin, mucous membrane, blood vessels of the brain and coronary arteries).
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PL 21838/0003

No new data were submitted nor were they necessary for this application, as the data are identical to that of the previously granted application for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

Since this product will be used in place of other products that are currently on the market, no increase in environmental exposure is anticipated. An Environmental Risk Assessment (ERA) is, therefore, not deemed necessary.

The manufacturing facilities are the same as for Nanogam 50 mg/ml solution for infusion (PL 16935/0004), as such this information has already been assessed, and GMP compliance is demonstrated by the provision of GMP certification.

A summary of the pharmacovigilance system has been provided with this application and is satisfactory.

A national licence was granted in the UK on 22 September 2011.

II QUALITY ASPECTS

LICENCE NO: PL 21838/0003

PROPRIETARY NAME: Aragam

ACTIVE(S): Human Normal Immunoglobulin

COMPANY NAME: Oxbridge Pharma Limited

E.C. ARTICLE: Article 8.3 of Directive 2001/83/EC for a known active substance (duplicate application)

LEGAL STATUS: Prescription-only medicine (POM)

II.1 INTRODUCTION

This is a National application, submitted under Directive 2001/83/EC Article 8(3), a full-dossier application for a known active substance. The quality, non-clinical and clinical data provided are identical to those approved for the product Nanogam 50mg/ml Solution for Infusion, which was approved in the UK to Stichting Sanquin Bloedvoorziening on 27 October 2010 (PL 16935/0004) following a mutual recognition procedure (FI/H/357/01/E/002).

II.2 MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Aragam 50 mg/ml solution for infusion. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Aragam is a solution for infusion. The solution is a clear or slightly opalescent, colourless or pale yellow.

Aragam is supplied in the following pack sizes 20 ml, 50 ml, 100 ml, 200 ml and 400 ml, containing 1 g, 2.5 g, 5 g, 10 g and 20 g of immunoglobulin, respectively. Not all sizes may be marketed.
2.3 Stability of the product
The proposed shelf-life is six 3 years with the special storage conditions of, “Store in a refrigerator (2°C-8°C)”, “Do not Freeze”, “Keep the vial in the outer carton in order to protect from light”. The product can be stored at or below 25°C up to six months, for example while travelling, without impairing its efficacy.

2.4 Legal status
On approval, the product will be available as a prescription-only medicine (legal status POM).

2.5 Marketing authorisation holder/Contact Persons/Company
Oxbridge Pharma Limited, 15 Fitzroy House, Lynwood Drive, Worcester Park, KT4 7AT, United Kingdom
The QP responsible for pharmacovigilance is stated

2.6 Manufacturers
The proposed manufacturing sites are consistent with those registered Nanogam 50 mg/ml solution for infusion (PL 16935/0004) and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.7 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

2.8 Manufacturing process
The proposed manufacturing process is consistent with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

2.9 Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

2.10 Drug substance specification
The proposed drug substance specification is consistent with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

2.11 TSE Compliance
For starting material of the drug substance, plasma of human origin, Albumin and other human tissue derived materials, the suppliers of human plasma are provided.

TSE issues
Product of human origin normal immunoglobulin
Pepsin porcine reagent
Lactose reagent
Milk reagent

TSE risk assessment for Nanogam has also been provided and is satisfactory.

2.12 Adventitious agents safety evaluation
Human plasma is the only biological starting material used in the manufacturing process of Aragam. Copies of updated PMF certificates are provided for Sanquin (EMEA/H/PMF/000007/04/AU/#, last update 19th February 2009), CAF-DCF (EMEA/H/PMF/000010/06/AU/#, last update 25th September 2008) and for Biotest Pharma GmbH (EMEA/H/PMF/000009/05/AU/#, last update 24th September 2009). The choice of blood donors is considered to be satisfactory.

The virus reduction/clearance steps in the production process have been validated. The studies confirmed acceptable virus clearance during the production process for Aragam.

II.3 EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

II.4 PRODUCT NAME AND APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is the same as the appearance of Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

II.5 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

II.6 PATIENT INFORMATION LEAFLET (PIL)/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

Carton and label
The carton and label have been prepared in-line with the details registered Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

II.7 CONCLUSIONS
The pharmaceutical data submitted is the same as for Nanogam 50 mg/ml solution for infusion (PL 16935/0004) granted to Stichting Sanquin Bloedvoorziening following an incoming mutual recognition repeat-use procedure (FI/H/357/01/E/002). The application is approvable from a quality perspective.
III NON-CLINICAL ASPECTS

Non-clinical studies have been conducted in addition to a review of the published data for human immunoglobulin. One safety pharmacology study (Study Report 041-041, Hypotensive effect study during the shelf life study of Nanogam) has been presented and has been previously reviewed in the assessment of Nanogam (PL 16935/0004); no concerns had been raised in relation to this procedure previously.

III.1 GLP ASPECTS

The assays for the hypotensive effect study (Study Report 041-041) were performed by Sanquin Blood Supply Foundation, Experimental Animal Facilities Department, Amsterdam, The Netherlands in compliance to GLP. For the published data it is not known whether the studies cited were conducted in accordance with the GLP regulations. However, it is assumed that the studies conducted would have been in compliance with the standards prevailing at the time.

III.2 PHARMACOLOGY

Brief summary

Immunoglobulins are normal constituents of the human body. Intact IgG plays a central role in immune defence system. The antibody spectrum in plasma reflects the immunity status of the body, as a result natural infections and effects of vaccinations. IgG binds antigens and thereby launches the effector functions which lead to the phagocytosis and lysis mechanisms of alloantigens or micro-organisms. The Fc part of the molecule acts as a transmitter of the major effector functions, complement activation and opsonization.

Vasoactive side effects and intravenous tolerance of immunoglobulins have been studied in animal models. The immediate side effects of intravenous immunoglobulin infusions, like chills, nausea, or decrease of blood pressure, are regarded to be mainly caused by IgG polymers, IgA, or prekallikrein activator (PKA) that might be present in the infused preparation. Nanogam (in this application, Aragam), complying with monograph 0918 of the European Pharmacopoeia has a low upper limit of acceptance for those substances.

Pharmacodynamics

There is extensive study of the primary pharmacodynamics of the active substance human plasma IgG in the clinical part. The clinical experience supersedes the findings from non-clinical studies.

Safety pharmacology

Study Report 041-041 was conducted to detect changes in blood pressure of animals treated with Nanogam (Aragam) stored for up 12 months at 37°C, 24 months at 25°C or 36 months at 2-8°C. Samples were taken from 10 production batches during stability (shelf life) studies. The blood pressure effects were studied at 0, 6 and 12 months storage at 37°C, at 0, 12 and 24 months at 25°C and at 0,12, 24 and 36 months at 2-8°C. The effect on blood pressure was tested in 2-3 female rats as an i.v. bolus of 250 mg/kg and an infusion rate of 6 ml/min (an approximate infusion rate of 0.1 ml/second). Recordings were made for a standard duration of 15 minutes after i.v. infusion. In each of the studies the concentration of immunoglobulin was 5%. None of the studied batches caused significant changes in the mean arterial pressure or heart rate either before or after storage for up to 36 months at 2-8°C. There seemed no hypotensive effect during the shelf-life study of Nanogam and is in line with the clinical studies showing no hypotensive results with Nanogam.
Pharmacodynamic drug interactions
No new data has been provided

Assessor’s overall conclusions on pharmacology
There is an extensive knowledge of human immunoglobulin in the clinic. The applicant has provided an additional safety pharmacology study in rats to study the hypotensive effects of Nanogam over the course of shelf-life, even after storage for 12 months at 37°C, 24 months at 25°C or 36 months at 2–8°C.

Pharmacokinetics
Non-clinical pharmacokinetic studies have not been described. The applicant has argued that clinical experience supersedes the findings from non-clinical studies. This is acceptable.

Toxicology
The product Aragam is composed of human IgG, a normal plasma constituent. Vasoactive side effects and intravenous tolerance of immunoglobulins have been studied in a limited number of animal models. Immediate side effects of intravenous immunoglobulin infusions, like chills, nausea, or decrease of blood pressure, are regarded to be mainly caused by IgG polymers, IgA, or PKA present in the infused preparation.

Immunoglobulins are normal constituents of the human body. Therefore, no traditional toxicity tests were performed. Single dose toxicity testing is of no relevance since higher doses result in overloading. Repeated dose toxicity testing and embryo-fetal toxicity studies are not informative due to induction of, and interference with, antibodies. Metabolism has not been tested in an animal model because Aragam is a human plasma product. Effects of the product on the immune system of the newborn have not been studied. In addition, clinical experience with intravenous immunoglobulins provides no indication for tumorigenic and mutagenic effects.

The very low levels of the S/D treatment related impurities TNBP and polysorbate 80 in Aragam are not expected to cause adverse effects. This conclusion in reached based both on theoretical consideration and the extensive clinical experience obtained with related S/D treated blood products.

Ecotoxicity/environmental risk assessment
No formal Environmental Risk Assessment has been provided. According to the guideline on the environmental risk assessment of medicinal products for human use, an environmental risk assessment (ERA) is required for all new marketing authorisation applications for a medicinal product including those through a decentralised procedure.

The applicant has argued that as Nanogam (Aragam) is a constituent from normal human blood and is used in a hospital setting or at home by patients themselves, the product can be discarded as normal household waste in accordance with local requirements. A proper justification for not performing an environmental risk assessment in accordance with the EU guideline (CHMP/SWP/4447/00) has been provided.

Assessor’s overall conclusions on toxicology
No traditional toxicity tests were performed as immunoglobulins are considered normal constituents of the human body. Clinical experience supersedes the findings of non-clinical findings. No concerns are raised in respect to treatment related impurities. A proper justification for not performing an environmental risk assessment in accordance with the EU guideline (CHMP/SWP/4447/00) has been provided.
ASSESSOR’S OVERALL CONCLUSIONS
Published literature and the new non-clinical data have been reviewed by Hannu Antero Raunio, a professor in Drug Toxicology, University of Kuopio (now University of Eastern Finland), Finland. The Expert has adequate experience of pharmacology and toxicology.

A review of the available non-clinical data has been submitted, supplemented with the applicant’s non-clinical data where appropriate. The Pharmaco-toxicological properties of human immunoglobulin have been well defined and extensive clinical experience has been gained.

Only a limited number of non-clinical tests have been performed with Nanogam (Aragam), which is considered as acceptable due to proteinaceous nature of the product and to its human origin. One safety pharmacology study has been conducted in the rat focusing on possible hypotensive effects of Nanogam. No significant changes in the mean arterial pressure or heart rate were observed. No traditional toxicity tests were performed.

There are no objections to the approval of human immunoglobulin from a non-clinical point of view.

IV. CLINICAL ASPECTS
The clinical data submitted is the same as for Nanogam 50 mg/ml solution for infusion (PL 16935/0004) granted to Stichting Sanquin Bloedvoorziening following an incoming mutual recognition repeat-use procedure (FI/H/357/01/E/002). The clinical evidence submitted is that generated for Nanogam and there is no new information.

The application can be approved from a clinical perspective.

V OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT
QUALITY
The important quality characteristics of Aragam 50 mg/ml solution for infusion are well defined and controlled. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-ClinICAL
The pharmaco-toxicological properties of human immunoglobulin have been well defined and extensive clinical experience has been gained. The non-clinical studies provided are adequate to support the application for Aragam 50 mg/ml solution for infusion.

EFFICACY AND SAFETY
The clinical evidence provided for Nanogam 50 mg/ml solution for infusion are sufficient to support the application for Aragam 50 mg/ml solution for infusion. The SmPC, PIL and labelling are acceptable.

BENEFIT-RISK ASSESSMENT
No new non-clinical or clinical safety concerns have been identified. Sufficient clinical experience with Nanogam 50 mg/ml solution for infusion is considered to have demonstrated the therapeutic value of Aragam 50 mg/ml solution for infusion. The benefit-risk balance is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC) and patient information leaflet (PIL) are consistent with those of the reference product. In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website. The mock-ups for the labelling approved with the national application PL 21838/0003-0001 are presented below:
Aragam® 50 mg/ml

Store at 2°C-8°C (ice-cooled) or in a refrigerator. Do not freeze. Keep the vial in the outer carton in order to protect from light.

Maximum storage period at room temperature (up to 25°C): up to 1 day. If the product is not used during the period, it must be discarded.

Keep out of the reach and sight of children. This product contains glucose.

Read the package leaflet before use.

Manufactured by:
Stichting Gabein Biopharmaceutics
Paviljoen 2, 5270
Amstelveen, NL-1086 CX,
The Netherlands.

Date to be stored at room temperature (at or below 25°C)

Aragam® 50 mg/ml Solution for infusion Human normal immunoglobulin

50 ml (= 2.5 g protein)

For intravenous use only

UKPAR Aragam 50 mg/ml solution for infusion

PL 21838/0003

Marketing Authorisation Holder:
Oxbridge Pharma Limited
11 Theobald House, Lyne Wood Drive
Waterlooville Park, Surrey, BTA 1A 7
United Kingdom

Marketing Authorisation Number:
PL 21838/0003
UKPAR Aragam 50 mg/ml solution for infusion
PL 21838/0003

For intravenous use only

Aragam™ 50 mg/ml
Solution for infusion
Human normal immunoglobulin

20 ml (= 1 g protein)

Read the package leaflet before use
This product contains glucose
UKAR Aragam 50 mg/ml solution for infusion

For Intravenous use only

**Aragam**™ 50 mg/ml
Solution for infusion
Human normal immunoglobulin

50 ml (= 2.5 g protein)

Read the package leaflet before use
This product contains glucose

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For Intravenous use only

**Aragam**™ 50 mg/ml
Solution for infusion
Human normal immunoglobulin

100 ml (= 5 g protein)

Read the package leaflet before use
This product contains glucose

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For Intravenous use only

**Aragam**™ 50 mg/ml
Solution for infusion
Human normal immunoglobulin

200 ml (= 10 g protein)

Read the package leaflet before use
This product contains glucose
For intravenous use only

**Aragam™ 50 mg/ml**
Solution for infusion

Human normal immunoglobulins

400 ml (= 20 g protein)

Read the package leaflet before use
This product contains glucose
Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

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<td>To update sections 2, 4.2, 4.3, 4.4, 4.6, 4.8, 6.5 and 6.6 of the SmPC in line with: 1. New quality data (update of the subclass distribution). 2. New clinical/pharmacovigilance data (including updates in line with the QRD template and Core SmPC).</td>
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Annex I

Reference:  PL 21838/0003 - 0031
Product:  ARAGAM 50 MG/ML SOLUTION FOR INFUSION
Marketing Authorisation Holder:  OXBRIDGE PHARMA LIMITED
Active Ingredients:  HUMAN NORMAL IMMUNOGLOBULIN

Reason:  To update sections 2, 4.2, 4.3, 4.4, 4.6, 4.8, 6.5 and 6.6 of the SmPC in line with:
1. New quality data (update of the subclass distribution).
2. New clinical/pharmacovigilance data (including updates in line with the QRD template and Core SmPC).

Background

The SmPC has been updated in order to be consistent with the details registered for Nanogam 50 mg/ml solution for infusion (PL 16935/0004).

1. New quality data (update of the subclass distribution).

Supporting Evidence

In line with the European monograph for Human normal immunoglobulin for intravenous administration, Nanogam finished product contains the IgG antibodies of normal subjects. It has a defined distribution of IgG subclasses which is stated on the label of the finished product.

IgG subclass distribution of the Nanogam 5 % was determined initially with a different method than the one used now. Although the product was not changed, it is required to update the distribution with the currently used method. Furthermore, routine production of Nanogam 10 % will be started soon. These two products have the same production process except different final dilution levels, which has no impact on the distribution of the IgG subclasses. As the two products are the same except for the final protein concentration, the available data for Nanogam 5 %, collected in the last 10 years, can be statistically evaluated and used for both products.

IgG subclass distribution of Nanogam finished product was calculated based on the results of Nanogam 5% finished product batches (n = 167). The subclass distribution was determined as average (average +/- 3SD):
- IgG1: 64.9 % (58.9-70.8%)
- IgG2: 31.8 % (25.7-38.0%)
- IgG3: 2.8 % (0.7-4.8%)
- IgG4: 0.5 % (0.3-0.7%)

The average data for IgG subclass distribution will be incorporated into the SmPC of Nanogam; with the average values +/- 3SD as an internal limit in order to assess changes in subclass distribution in the future.

Moreover, 10 Nanogam 10 % finished products were tested for IgG subclasses. It was observed that the available batches of Nanogam 10% are within the limits determined.
Conclusion

A new method is used for the determination of the IgG subclass distribution; hence, the Company has performed a study that aims to re-determine the IgG subclass distribution for Nanogam using the current methods with data obtained over the last 10 years. As pointed out by the Company, there is no international standard available for IgG subclass distribution and the concentration of IgG3 and IgG4 measured with different reagents varies to some extent. The new study successfully determined the product’s IgG subclass distribution. This is acceptable.

Overall, the introduction of the Company’s new method for determination of IgG subclass distribution is not expected to have an effect on the quality of the product.

From a quality perspective, this variation (which also involves clinical assessment) is approvable.

2. New clinical/pharmacovigilance data (including updates in line with the QRD template and Core SmPC).

Supporting Evidence

The variation data submitted is that generated for Nanogam 50 mg/ml solution for infusion (PL 16935/0004) which has been previously assessed, there is no additional new information.

Conclusion

The application can be approved from a clinical perspective concerning changes with respect to sections 4.2, 4.3 and 4.6 of the SmPC and sections 1, 2, and 3 of the PIL.

SmPCs and a PIL have been updated satisfactorily.

The Summary of Product Characteristics (SmPC) and patient information leaflet (PIL) are consistent with those of Nanogam 50 mg/ml solution for infusion (PL 16935/0004). In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Decision - Granted
Date - 26 September 2016