SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Macimorelin 60 mg granules for oral suspension in sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 60 mg macimorelin (as acetate). 1 mL of the reconstituted suspension contains 500 micrograms macimorelin.

Excipient(s) with known effect

Contains lactose monohydrate 1,691.8 mg per sachet.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Granules for oral suspension in sachet.
White to off-white granules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
Macimorelin is indicated for the diagnosis of growth hormone deficiency (GHD) in adults (see section 5.1).

4.2 Posology and method of administration

The use of MACIMORELIN must be supervised by a physician or healthcare professional experienced in diagnosing growth hormone deficiency.

Posology

Adult population
The dose is calculated based on the patient´s body weight. The recommended single dose of the reconstituted suspension is 500 micrograms macimorelin per kg body weight.
The growth hormone release is to be evaluated with three blood samples collected at 45, 60 and 90 minutes after the administration of the medicinal product.

Discontinuation of therapy with growth hormone (GH) or medicinal products directly affecting the pituitary secretion of somatotropin
Patients on replacement therapy with growth hormone (GH, somatotropin) or on medicinal products directly affecting the pituitary secretion of somatotropin (e.g. somatostatin analogues, clonidine, levopoda and dopamine agonists) should be advised to discontinue such treatment at least 1 month before receiving macimorelin. These substances could lead to unreliable GH stimulation results (see also section 4.4 and 4.5).

Renal and/or hepatic impairment
The safety and efficacy of macimorelin in patients with renal and/or hepatic impairment have not been established (see also section 5.2). No data are available. If macimorelin is administered to patients with renal and/or hepatic impairment, the potential for an increased macimorelin plasma concentration cannot be excluded. It is unknown whether this may affect QTc. Therefore, ECG controls may be indicated prior to the administration of macimorelin and 1 hour, 2 hours, 4 hours and 6 hours after administration of macimorelin (see also section 4.4). Based on current understanding, this potential is unlikely to decrease the specificity of the test.

Elderly
Growth hormone secretion normally decreases with age. The efficacy of macimorelin in patients aged over 65 years has not been established. In patients with age up to 60 years, diagnostic performance of MAC and ITT were comparable. In the age group 60 years up to 65 years, the limited data available do not indicate the need for a separate cut-off point.

Paediatric population
The safety and efficacy of macimorelin in children and adolescents below 18 years have not yet been established (see also section 5.2). No data are available.

<u>Method of administration</u>

Oral use
MACIMORELIN granules are to be reconstituted with water and must be used within 30 minutes after preparation. Reconstituted suspension should be administered orally to patients fasting for at least 8 hours and who did not have strenuous physical exercises 24 hours before the test, since both could affect growth hormone levels.
The number of test sachets needed is based on body weight. One sachet will be required for a patient $\leq$ 120 kg, two sachets will be required if the patient

weighs more than 120 kg. The entire contents of one sachet is dissolved in 120 mL, and two sachets are dissolved in 240 mL, as applicable.
The volume of suspension in mL needed for the recommended macimorelin dose of 0.5 mg/kg equals the patient's body weight in kg. For example, a 70 kg patient will require 70 mL of the macimorelin suspension.

Assessment of fasted condition and lack of prior strenuous physical exercise
Before using MACIMORELIN it is important to ensure that the patient is in fasting condition for at least 8 hours and did not have strenuous physical exercises 24 hours before the test, since both could affect GH levels. If either of these conditions is not met, the growth hormone stimulation test must be re-scheduled for a new test day.
During the test, the patient needs to stay fasted until the end of the blood sampling. Fluid intake of no more than 100 mL of non-carbonated water is allowed each within 1 hour pre-dose, as well as within 1 hour post-dose (see section 4.4).

Long-term use

Macimorelin is indicated as a single-dose diagnostic test. No information is available on the safety and effects of macimorelin during long-term use.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Interpretation of macimorelin test results

Clinical studies have established that a maximally stimulated serum GH level of less than 2.8 ng/mL (at the 45, 60 and 90 minutes timepoints) following macimorelin administration confirms a diagnosis of adult growth hormone deficiency. As with all GH stimulation tests, also the macimorelin test results should always be interpreted on basis of the outcome of all examinations within the diagnostic work-up for a patient.

The safety and diagnostic performance of macimorelin have not been established for patients with BMI > 40 kg/m^2. Macimorelin induced GH release was lower in patients with higher BMI. In patients with high BMI up to 40 kg/m^2, diagnostic performance of MAC and of ITT were comparable.

The cut-off point for macimorelin has not been established in the transition period from late puberty to full adult maturation. In patients between 18 and 25 years of age, the diagnostic performance of MAC and of ITT were comparable.

QTc prolongation

During clinical development, two transient ECG abnormalities were observed in one test subject and reported as serious possibly adverse reactions. These ECG abnormalities consisted of T wave abnormalities and QT prolongation.

Macimorelin causes an increase of about 11 ms in the corrected QT (QTc) interval by an unknown mechanism (see also section 5.1). QT prolongation can lead to development of torsade de pointes-type ventricular tachycardia with the risk increasing as the degree of prolongation increases. The concomitant use with medicinal products that are known to induce torsades de pointes should be avoided (see also section 4.5). Macimorelin should be used with caution in patients with proarrhythmic condition (e.g., history of myocardial infarction, heart failure or prolonged ECG QTc interval, as defined as QTc > 500 ms). For such patients, ECG controls may be indicated prior to the administration of macimorelin and 1 hour, 2 hours, 4 hours and 6 hours after administration of macimorelin. In patients with known congenital or acquired long QT syndrome and in patients with a history of torsades de pointes, the use of macimorelin may only be considered in a cardiovascular clinical unit.

Discontinuation of therapy with growth hormone (GH) or medicinal products directly affecting the pituitary secretion of somatotropin

Patients on replacement therapy with growth hormone (GH, somatotropin) or on medicinal products directly affecting the pituitary secretion of somatotropin (e.g. somatostatin analogues, clonidine, levopoda and dopamine agonists) should be advised to discontinue such treatment at least 1 month before receiving a test dose of macimorelin. Exogenous GH or medicinal products directly affecting the pituitary gland could influence the somatotropic function of the pituitary gland and lead to unreliable GH stimulation results (see also section 4.2 and section 4.5).

Patients with a deficiency affecting hormones other than growth hormone (GH)

Patients with a deficiency affecting hormones other than GH (e.g. adrenal, thyroidal and/or gonadal insufficiency, diabetes insipidus) should be adequately replaced with the other deficient hormones before any testing for a deficiency of GH stimulation is performed, to exclude a stimulation failure due to a secondary GH deficiency.

Patients with Cushing’s disease or on supra-physiologic glucocorticoid therapy

Hypercortisolism has a significant impact on the hypothalamic-pituitary-adrenal axis. Therefore, the diagnostic performance of the test may by affected in patients with Cushing's disease or on supra-physiologic glucocorticoid therapy (e.g. systemic administration of doses of hydrocortisone (or its equivalent) in excess of 15 mg/m^2/day) and lead to false positive test results.

Potential for increased oral bioavailability and macimorelin plasma concentration with use of strong CYP3A4/P-gp-inhibitors

Drug-drug interaction studies with CYP3A4/P-gp-inhibitors have not been conducted.
A potential for increased oral bioavailability and macimorelin plasma concentration with use of strong CYP3A4/P-gp-inhibitors cannot be excluded. It is unknown whether such potential interactions may also affect QTc (see above). Based on current understanding, this potential is unlikely to decrease the specificity of the test.

Potential for false positive test results with use of strong CYP3A4 inducers

Concomitant use of strong CYP3A4 inducers with MACIMORELIN can decrease macimorelin plasma levels significantly and thereby lead to a false positive result (see also section 4.5). Strong CYP3A4 inducers should be discontinued and a washout time of five elimination half-lives should be considered prior to test administration.

Potential for false negative test results in recent onset hypothalamic disease

Adult growth hormone (GH) deficiency caused by a hypothalamic lesion may not be detected early in the disease process. Macimorelin acts downstream from the hypothalamus and macimorelin stimulated release of stored GH reserves from the anterior pituitary could produce a false negative result early when the lesion involves the hypothalamus. Repeat testing may be warranted in this situation.

Information about lactose and sodium

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should take this medicinal product only if the expected benefit of the test clearly outweighs the potential risk associated with an intake of maximum 1,691.8 mg lactose per sachet.
This medicinal product contains less than 1 mmol sodium (23 mg) per sachet that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Macimorelin is metabolised mainly by CYP3A4 *in vitro*.
Co-administration of a CYP3A4 inhibitor may increase the macimorelin plasma concentration, and this, in turn, could yield higher plasma GH levels. Based on current understanding, this is unlikely to decrease the specificity of the test.

Administration of a CYP3A4 inducer (such as carbamazepine, dabrafenib, efavirenz, enzalutamide, eslicarbazepine, fosphenytoin, lumacaftor, modafinil, nevirapine, oxcarbazepine, phenobarbital, phenytoin, pioglitazone, pitolisant, primidone, rifabutin, rifampicin and St John's wort (*Hypericum perforatum*)) may reduce the plasma macimorelin concentrations and may affect the diagnostic performance of the test and therefore should be avoided. A sufficient washout time of five elimination half-lives of the CYP3A4 inducer prior to administration of the test is recommended (see section 4.2 and section 4.4).

No drug-drug interaction studies have been performed in humans.

Medicinal products affecting growth hormone release

The following medicinal products may impact the accuracy of the diagnostic test. Concomitant use is to be avoided with (see also section 4.2 and section 4.4):

- Medicinal products that directly affect the pituitary secretion of growth hormone (such as somatostatin, insulin, glucocorticoids, and cyclooxygenase inhibitors such as acetylsalicylic acid or indometacin).
- Medicinal products that may transiently elevate growth hormone concentrations (such as clonidine, levodopa, and insulin).
- Medicinal products that may blunt the growth hormone response to macimorelin (such as muscarinic antagonists: atropine, anti-thyroid medicinal products: propylthiouracil and growth hormone medicinal products).
- Growth hormone medicinal products should be discontinued at least 1 month before administering macimorelin.
  Sufficient washout time (five elimination half-lives) of medicinal products prior to administration of macimorelin is recommended.

Medicinal products with a potential to induce torsades de pointes

Co-administration of macimorelin with medicinal products with a potential to induce torsades de pointes (antipsychotic medicinal products e.g. chlorpromazine, haloperidol, antibiotics (e.g., moxifloxacin, erythromycin, clarithromycin), anti-arrhythmics Class Ia (e.g. quinidine), and Class III (e.g. amiodarone, procainamide, sotalol) or any other medicinal products that may induce torsades de pointes) should be avoided (see section 4.4).

4.6 Fertility, Pregnancy and lactation

Women of childbearing potential
Women of childbearing potential must use adequate contraceptive methods at the time when macimorelin will be administered.

Pregnancy
There are no data for the use of macimorelin in pregnant women. Studies in animals are insufficient with respect to reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Macimorelin is not recommended during pregnancy.

Breast-feeding
It is unknown whether macimorelin or its metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to abstain from macimorelin, taking into account the benefit of breast-feeding for the child and the benefit of the test for the woman.

Fertility
There are no data available on animal (see section 5.3) or human male and female fertility.

4.7 Effects on ability to drive and use machines

MACIMORELIN has minor influence on the ability to drive and use machines.
Dizziness has been reported by some patients taking macimorelin. In case a patient should be reporting dizziness as side effect, the patient should be instructed to neither drive nor use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions associated with MACIMORELIN reported in Study 052 (see section 5.1) in 154 patients were dysgeusia (5%), headache fatigue, nausea (each 3%), dizziness (2%), as well as abdominal pain, diarrhoea, feeling hot, feeling cold, hunger, palpitations, sinus bradycardia, somnolence, thirst, tremor, and vertigo (each 1%). Overall, the adverse reactions reported were mostly of mild intensity and short duration without a specific treatment need.

Tabulated list of adverse reactions

Adverse reactions reported in Study 052 are listed below by MedDRA body system organ class and by frequency: 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); not known (cannot be estimated from available data).

MedDRA organ class	Common	Uncommon	Not known
Nervous system disorders	Dysgeusia (bitter/metallic taste) Dizziness Headache	Somnolence Tremor	
Ear and labyrinth disorders		Vertigo	
Cardiac disorders		Palpitations Sinus bradycardia	ECG QT prolonged ECG T wave abnormal
Gastrointestinal disorders	Nausea Diarrhoea	Abdominal pain	
General disorders and administration site conditions	Fatigue Feeling hot	Feeling cold Hunger Thirst	

Description of selected adverse reactions

Cardiac electrophysiology
During clinical development, two transient ECG abnormalities were observed in one test subject and reported as serious possibly adverse reactions. These ECG abnormalities consisted of T wave abnormalities and QT prolongation (see also section 4.4).

The effects of macimorelin on ECG parameters were investigated in a dedicated Thorough QT study of a supra-therapeutic dose of macimorelin (2 mg/kg) and in a single-ascending dose study, which included three dose levels of macimorelin (0.5 mg/kg, 1 mg/kg and 2 mg/kg). Macimorelin causes an increase of about 11 ms in the corrected QT (QTc) interval (see section 5.1). The mechanism for the observed QTcF prolongation is unknown.

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 via Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No specific recommendations after overdose are given. In the event of an overdose, symptomatic and supportive measures should be employed. Further possible undesirable effects in case of overdosing could include headache, nausea, vomiting and diarrhoea. In patients with a QTc > 500 ms, an ECG monitoring should be applied (see section 4.4 and 5.1).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic agents, Tests for pituitary function, ATC code: V04CD06

Mechanism of action

Macimorelin is an orally available peptidomimetic with growth hormone (GH) secretagogue activity similar to ghrelin. Macimorelin stimulates GH release by activating growth hormone secretagogue receptors (GHSR) present in the pituitary and hypothalamus.

Pharmacodynamic effects

GH stimulation
In dose finding studies in healthy subjects, maximum stimulation of GH secretion was achieved following single dose administration of 0.5 mg/kg macimorelin. Maximum GH levels have been observed approximately 45 to 60 minutes after administration of macimorelin.
In a diagnostic study comparing macimorelin with the insulin tolerance test (ITT) stimulated GH concentrations after macimorelin were on average 1.4 fold higher than in the ITT.

Cardiac electrophysiology

The effects of macimorelin on ECG parameters were investigated in a dedicated Thorough QT study that investigated in a 3-way cross-over design with 60 healthy subjects the effects of a supra-therapeutic dose of macimorelin

(2 mg/kg, i.e., 4 times the recommended dosage) in comparison with placebo and with moxifloxacin. This study showed a mean baseline- and placebo-adjusted change (upper single-sided 95% confidence interval) in QTcF of 9.6 ms (11.4 ms) at 4 h post-dose (see also section 4.4), which occurred after the mean maximum macimorelin plasma concentration (0.5 h). A similar increase in the QTcF interval was also observed in a single-ascending dose study, which included three dose levels (0.5 mg/kg, 1 mg/kg and 2 mg/kg (2 times and 4 times the recommended dosage, respectively)). All three dose levels studied showed a similar magnitude of QTcF prolongation in the Thorough QT study, suggesting an absence of dose dependent changes. The mechanism for the observed QTcF prolongation is unknown.

Clinical efficacy and safety

The diagnostic efficacy of MACIMORELIN was established in a randomized, open-label, single dose, cross-over study (AEZS-130-052) comparing the level of agreement between the macimorelin test (MAC) results and insulin tolerance test (ITT) results. Four groups of individuals were evaluated: three groups of adult patients with different pre-test probability of growth hormone deficiency (Group A (high likelihood), Group B (intermediate likelihood), Group C (low likelihood) and healthy control subjects (Group D)).

For both the ITT and the MAC test, serum concentrations of GH were measured at 30, 45, 60 and 90 minutes after administration. The test was considered positive (i.e., growth hormone deficiency (GHD) diagnosed) if the maximum serum GH level observed after stimulation was less than the pre-specified cut-off point of 2.8 ng/mL for the MAC test or 5.1 ng/mL for the ITT.

GH levels were determined centrally with the IDS-iSYS assay (Immunodiagnostic Systems Ltd., UK).

The level of negative and positive agreement between the results of the ITT and the MAC test was used to evaluate the performance of the MAC test. Negative agreement is the proportion of subjects with a negative ITT (i.e., those who do not have GHD per the ITT) who also have a negative MAC test. With a high level of negative agreement, the MAC test will not wrongly diagnose an individual without GHD per the ITT as having GHD. Positive agreement is the proportion of subjects with a positive ITT (i.e., those who have GHD per the ITT) who also have a positive macimorelin test. With a high level of positive agreement, the MAC test will not wrongly diagnose an individual with GHD per the ITT as not having GHD.

Sensitivity and specificity for both growth hormone stimulation tests (GHSTs) were estimated, assuming all high likelihood AGHD subjects of Group A as ‘true’ AGHD subjects and all healthy matching subjects of Group D as ‘true’ AGHD negative subjects.

Results

One hundred and fifty-seven (157) subjects underwent at least one of the two tests in this study, 59% were male, 41% female and 86% of white origin. The median age was 41 years (range: 18 - 66 years) and body mass index 27.5 kg/m^2 (range: 16 – 40 kg/m^2). Data on both tests were available for 140 subjects; 38 (27%) in Group A, 37 (26%) in Group B, 40 (29%) in Group C and 25 (18%) in Group D. One out of 154 MAC tests (0.6%) performed failed due to a technical error and 27 out of 157 ITTs (17.2%) performed failed because induction of severe hypoglycemia (i.e., the stimulus) could not be achieved.

The estimates for negative and positive agreement between MAC and the ITT in the overall study population were 94% and 74% with lower 95% confidence interval bounds 85% and 63%, respectively. Negative and positive agreement between MAC and the ITT in subjects with intermediate or low risk (Groups B and C) were 93% and 61% with lower 95% confidence interval bounds 80% and 43%, respectively. These results are based on peak GH values (maximum GH concentrations across all measurement timepoints).

Point estimates for sensitivity ranged from 0.87 to 0.90 for the MAC and from 0.97 to 1.0 for the ITT, depending on the inclusion or exclusion of data from not matched Group A subjects, respectively. For both GHSTs, the estimated specificity was 0.96, irrespective of the in/exclusion data from not matched Group A subjects.
Repeatability was tested in a subset of 34 subjects who underwent two MAC tests. Agreement between the result of the first test and the second test was observed in 31 cases (91.2%).

Post-hoc analysis with a cut-off point of 3.0 ng/mL for the ITT

An exploratory analysis was conducted on the performance of the MAC based on an ITT cut-off point of 3.0 ng/mL. The estimates for negative and positive agreement were 95% and 86% with lower 95% confidence interval bounds 87% and 75%, respectively. Repeatability was 97%. Point estimates for sensitivity and specificity were 87% and 96% from not matched Group A subjects, respectively.

Both co-primary endpoints as pre-defined in Study 052 (lower limit of the 95% CI for negative agreement ≥ 75%, lower limit of the 95% CI for positive agreement ≥ 70%) are met when using an ITT cut-off point of 3.0 ng/mL and the pre-defined cut-off point for the MAC of 2.8 ng/mL.

Paediatric population

The EMA has deferred the obligation to submit the results of studies with MACIMORELIN in one or more subsets of the paediatric population in the diagnosis of growth hormone deficiency (see section 4.2 for information on paediatric use).

Elderly

The pharmacodynamics of macimorelin was not sufficiently evaluated in the elderly population aged > 65 years.

5.2 Pharmacokinetic properties

Absorption

Macimorelin was absorbed rapidly and the maximum plasma macimorelin concentrations (C_{max}) were observed approximately 30 minutes to 1 hour and 10 minutes after oral administration of 0.5 mg/kg macimorelin after fasting for at least 8 hours. A liquid meal decreased the macimorelin C_{max} and AUC by 0.42 and 0.5 fold, respectively.

The oral bioavailability may be limited (among others) by first pass metabolism via CYP3A4 (see section 4.5).

Distribution

Macimorelin is moderately bound to plasma proteins. Plasma protein binding decreases with increasing concentrations from 78% at 0.1 µM to 62% at 10 µM. At the clinically relevant concentration of 0.1 µM (clinical C_{max} = 11.2 ng/ml = approx. 0.02 µM), the unbound fraction of macimorelin in human plasma is 22%.

Biotransformation

CYP3A4 is the major enzyme to metabolize macimorelin. Studies to detect macimorelin metabolites did not identify any metabolites.

Elimination

An *in vitro* human liver microsomes study showed that CYP3A4 is the major enzyme to metabolize macimorelin.
Macimorelin was eliminated with a mean terminal half-life ($T_{1/2}$) of 4.1 hours.

PK/PD relationship

Macimorelin showed a dose-dependent release of GH after oral dosing. A dose of 0.5 mg/kg macimorelin was shown to induce maximal GH release. Maximal GH release has been observed at macimorelin plasma concentrations of $\geq$ 7 ng/mL.

Special populations

No studies have been conducted to evaluate the pharmacokinetics of macimorelin in paediatric patients or in patients with renal or hepatic impairment. Only limited pharmacokinetic data are available in the elderly.

5.3 Preclinical safety data

Preclinical data from safety pharmacology, repeated dose toxicity and genotoxicity studies reveal no specific hazard for humans. No studies to assess carcinogenicity and effects on reproduction and development have been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Colloidal anhydrous silica
Crospovidone type A
Saccharin sodium dihydrate
Sodium stearyl fumarate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened sachet

The shelf life of a sachet is 5 years.

Reconstituted suspension

The suspension must be administered within 30 minutes after preparation. Residual suspension must be discarded according to local regulations.

6.4 Special precautions for storage

Store in the original package, in order to protect from light and moisture.
Store in a refrigerator (2°C - 8°C).
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

One LDPE/Alu/LDPE/paper sachet containing 1,817 mg granules placed in cardboard box.

Each cardboard box contains 1 sachet.

6.6 Special precautions for disposal

The suspension must be prepared and administered by a healthcare professional.

Items needed: MACIMORELIN sachet, tap water in decanter, graduated glass or transparent plastic container, stirring device, 50 mL graduated syringe without needle, drinking glass

Step 1
Weigh the patient.

Step 2
Determine the number of test sachets needed based on body weight: one sachet will be required for a patient weighing up to 120 kg, two sachets will be required if the patient weighs more than 120 kg.

Step 3
Add required volume of water in a graduated glass or transparent plastic container. Dissolve the entire contents of the sachet in water: one sachet in 120 mL, two sachets in 240 mL, as applicable.

Stir the suspension gently for 2 minutes (a small amount of undissolved particles will remain giving a slightly turbid suspension). The suspension should be stirred until it is slightly turbid without particles at the bottom of the container. The suspension should be stirred again, when some particles settle at the bottom of the container for example after the suspension is left standing for some time.

Step 4
Determine the volume of suspension needed for the recommended macimorelin dose of 0.5 mg/kg. The suspension volume in mL equals the patient's body weight in kg. For example, a 70 kg patient will require 70 mL of the macimorelin suspension.

Measure the required volume using a 50 mL graduated syringe without a needle.

Transfer the measured amount to a drinking glass.

Step 5
Have the patient drink the entire content of the drinking glass within 30 seconds.

The suspension must be used within 30 minutes after preparation. Any suspension that remains must not be stored and must be discarded.

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

Step 6
Draw venous blood samples for growth hormone determination at 45, 60 and 90 minutes after administration.

Step 7
Prepare plasma or serum samples and send to a laboratory for growth hormone determination.

7 MARKETING AUTHORISATION HOLDER

Atnahs Pharma UK Limited.

Sovereign House

Miles Gray Road

Basildon, Essex

SS14 3FR

United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 43252/0050

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/01/2024

10 DATE OF REVISION OF THE TEXT

12/01/2024