1.7 Summary of Product Characteristics (SPC)

1. NAME OF THE MEDICINAL PRODUCT

MENOTAS HP 150

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MENOTAS HP 150
Each vial contains:
Menotropin BP equivalent to activity of
Follicle Stimulating Hormone 150 IU
Luteinising Hormone 150 IU
Excipients: Q.S.
Reconstitute with 1 ml of Sodium Chloride Injection BP (0.9% w/v)

3. PHARMACEUTICAL FORM

Powder for injection; and solvent for parenteral use.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Women:
- Anovulation, including polycystic ovarian disease (PCOD), in women who have been unresponsive to treatment with clomiphene citrate.
- Controlled ovarian hyperstimulation to induce the development of multiple follicles for assisted reproductive technologies (ART)

Selection of Patients
1. A thorough gynecologic and endocrinologic evaluation, including an assessment of pelvic anatomy must be performed before treatment with Menotropin. Patients with tubal obstruction should receive Menotropin only if enrolled in an IVF program.
2. Primary ovarian failure should be excluded by the determination of gonadotrophin levels.
3. Careful examination should be made to rule out the presence of an early pregnancy.
4. Patients in late reproductive life have a greater predilection to endometrial carcinoma as well as a higher incidence of anovulatory disorders. A thorough diagnostic evaluation should always be performed in patients who demonstrate abnormal uterine bleeding or other signs of endometrial abnormalities before starting Menotropin therapy.
5. Evaluation of the partner's fertility potential should be included in the workup.

Men:
Hypogonadotrophic hypogonadism in men: Menotropin with concomitant human chorionic gonadotropins therapy is indicated for the stimulation of spermatogenesis in men who have primary or secondary hypogonadotrophic hypogonadism.

4.2 Posology and method of administration

Dosage

Anovulatory infertility:

The dosage and schedule of treatment must be determined according to the needs of each patient. Response is monitored by studying the patient's serum estradiol levels and vaginal ultrasound visualization of follicles. Menotropin for injection may be given daily which should be maintained for 7 days by subcutaneous or intramuscular injection to provide a dose of 75 to 150 IU/day, and gradually adjusted if necessary until an adequate response is achieved, followed after 1 day by human chorionic gonadotropins. In menstruating patients, treatment should be started on the 4th/5th day of the menstrual cycle. The treatment course should be abandoned if no response is seen. Once adequate follicular development is evident, administration of Menotropin is stopped, and ovulation may then be induced by administering human chorionic gonadotropins (hCG) at a dose of 5000 -10000 IU. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy. This should reduce the chance of developing ovarian hyperstimulation syndrome (OHSS).

Assisted Reproductive Technologies

The recommended initial dose of Menotropin for injection for patients who have received a GnRH agonist for pituitary suppression is 150 to 300 IU/day. Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every two days and should not exceed 150 IU per adjustment. The maximum daily dose of Menotropin for injection given should not exceed 450 IU.

Once adequate follicular development is evident, hCG should be administered to induce final follicular maturation in preparation for oocyte retrieval. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy.

This should reduce the chance of developing OHSS.

Hypogonadotrophic hypogonadism in men

Spermatogenesis is stimulated with chorionic gonadotropins (1000 – 2000 IU two to three times a week) and then Menotropin for injection is given in a dose of 75 or 150 IU two or three times weekly. Treatment should be continued for at least 3 or 4 months.

Administration

Reconstitute with 1ml of Sodium Chloride Injection BP (0.9% w/v) provided in this pack and administer subcutaneously or intramuscularly immediately. Any unused reconstituted material should be discarded. Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration, whenever solution and container permit

4.3 Contraindications

Men and Women

1. Tumours of the pituitary or hypothalamic glands
2. Hypersensitivity to the active substance or any of the excipients used in the formulation

Women who have:

1. A high FSH level indicating primary ovarian failure.
2. Uncontrolled thyroid and adrenal dysfunction.
3. An organic intracranial lesion such as a pituitary tumor.
4. Sex hormone dependent tumors of the reproductive tract and accessory organs.
5. Abnormal uterine bleeding of undetermined origin.
6. Ovarian cysts or enlargement not due to polycystic ovary syndrome.
7. Menotropin for injection is not indicated in women who are pregnant. There are limited human data on the effects of Menotropin when administered during pregnancy.

Men

1. Tumours in the testes
2. Patients primary testicular failure are usually unresponsive to Menotropin and hCG therapy.
3. Prostate carcinoma

4.4 Special warnings and special precautions for use

Menotropin for injection is a drug that should only be used by physicians who are thoroughly familiar with infertility problems. It is a potent gonadotropic substance capable of Ovarian Hyperstimulation Syndrome (OHSS) in women with or without pulmonary or vascular complications. Gonadotrophin therapy requires a certain time commitment by physicians and supportive health professionals, and its use requires the availability of appropriate monitoring facilities.

Overstimulation of the ovary during Menotropin therapy

Ovarian Enlargement: Mild to moderate uncomplicated ovarian enlargement which may be accompanied by abdominal distension and/or abdominal pain occurs in approximately 5 to 10 % of women treated with Menotropin and hCG, and generally regresses without treatment within two or three weeks. The lowest dose consistent with expectation of good results and careful monitoring

of ovarian response can further minimize the risk of overstimulation.
If the ovaries are abnormally enlarged or the serum estradiol concentration is excessively elevated on the last day of Menotropin for injection therapy, hCG should not be administered in this course of treatment; this will reduce the chances of development of the Ovarian Hyperstimulation Syndrome (OHSS). In the event of hyperstimulation, the patient should refrain from sexual intercourse or to use barrier contraception methods for at least 4 days.
OHSS: OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS may progress rapidly to become a serious medical event. It is characterized by an apparent dramatic increase in vascular permeability which can result in a rapid accumulation of fluid in the peritoneal cavity, thorax, and potentially, the pericardium. The early warning signs of development of OHSS are severe pelvic pain, nausea, vomiting, and weight gain.The following symptomatology has been seen with cases of OHSS: abdominal pain, abdominal distension, gastrointestinal symptoms including nausea, vomiting and diarrhea, severe ovarian enlargement, weight gain, dyspnea, and oliguria. Clinical evaluation may reveal hypovolemia, hemoconcentration, electrolyte imbalances, ascites, hemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events.
Transient liver function test abnormalities suggestive of hepatic dysfunction, which may be accompanied by morphologic changes on liver biopsy, have been reported in association with the OHSS.
A physician experienced in the management of the syndrome, or who is experienced in the management of fluid and electrolyte imbalances, should be consulted.

Pulmonary and Vascular Complications

Serious pulmonary conditions (e.g. atelectasis, acute respiratory distress syndrome) have been reported. In addition, thromboembolic events both in association with, and separate from, the OHSS have been reported following Menotropin therapy. In women with generally recognised risk factors for thromboembolic events, such as personal or family history, treatment with gonadotropins may further increase the risk.

Multiple Pregnancies

The patient and her partner should be advised of the potential risk of multiple births before starting treatment.
Pregnancy wastage: Pregnancy wastage by miscarriage is higher in patients undergoing stimulation of follicular growth for ART procedures than in the normal population. The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies.

4.5 Interaction with other medicinal products and other forms of interaction

No drug/drug interaction studies have been conducted with Menotropin in humans.

4.6 Pregnancy and lactation

Menotropin should not be given during pregnancy. It is Pregnancy Category X drug. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if Menotropin are administered to a nursing woman.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

The adverse events occurring at an incidence of > 2 % in women treated with Menotropin are listed as below.
Body as a whole: Abdomen enlarged, Abdominal cramps, Abdominal fullness, Abdominal pain, Headache, Injection site pain, Injection site reaction, Malaise, Pain.
Digestive: Constipation, Diarrhea, Nausea, Vomiting, Nervous System: Dizziness
Respiratory: dysponea
Urogenital: Breast tenderness, Hot flash, OHSS, Pelvic discomfort, Post retrieval pain. Very rare cases of allergic reactions, localised or generalised, and hypersensitivity have been reported after treatment with gonadotropin containing products

4.9 Overdosage

The acute toxicity of menotrophin has been shown to be very low. However, too high a dosage for more than one day may lead to hyperstimulation, which is categorised as mild, moderate or severe. Symptoms of overdosage usually appear 3 - 6 days after treatment with human chorionic gonadotrophin.
Mild hyperstimulation - Symptoms include some abdominal swelling and pain, ovaries enlarged to about 5cm diameter. Therapy - rest; careful observation and symptomatic relief. Ovarian enlargement declines rapidly.
Moderate hyperstimulation - Symptoms include more pronounced abdominal distension and pain, nausea, vomiting, occasional diarrhoea, ovaries enlarged up to 12cm diameter. Therapy - bed rest; close observation especially in the case of conception occurring, to detect any progression to severe hyperstimulation.
Pelvic examination of enlarged ovaries should be gentle in order to avoid rupture of the cysts. Symptoms subside spontaneously over 2 - 3 weeks.
Severe hyperstimulation - This is a rare but serious complication - symptoms include pronounced abdominal distension and pain, ascites, pleural effusion, decreased blood volume, reduced urine output, electrolyte imbalance and

sometimes shock, ovaries enlarge to in excess of 12cm diameter. Therapy - hospitalisation; treatment should be conservative and concentrate on restoring blood volume and preventing shock. Acute symptoms subside over several days and ovaries return to normal over 20 - 40 days if conception does not occur - symptoms may be prolonged if conception occurs.

5.0 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Menotrophin is a gonadotrophin extracted from the urine of postmenopausal women and having both luteinising hormone and follicle stimulating hormone activity. It is given by intramuscular or subcutaneous injection in the treatment of male and female infertility.

Menotrophin (HMG) directly affects the ovaries and the testes. HMG has a gametropic and steroidogenic effect.

In the ovaries, the FSH-component in HMG induces an increase in the number of growing follicles and stimulates their development. FSH increases the production of oestradiol in the granulosa cells by aromatising androgens that originate in the Theca cells under the influence of the LH-component.

In the testes, FSH induces the transformation of premature to mature Sertoli cells. It mainly causes the maturation of the seminal canals and the development of the spermatozoa. However, a high concentration of androgens within the testes is necessary and can be attained by a prior treatment using hCG.

5.2 Pharmacokinetic properties

HMG is not effective when taken orally and is injected either intramuscularly or subcutaneously. The biological effectiveness of HMG is mainly due to its FSH content. The pharmacokinetics of HMG following intramuscular or subcutaneous administration show great individual variation. The maximum serum level of FSH is reached approximately 18 hours after intramuscular injection and 12 hours after subcutaneous injection. After that, the serum level decreases by a half-life of approximately 55 hours following intramuscular administration and 50 hours following subcutaneous administration.

Excretion of HMG, following administration, is predominantly renal.

5.3 Preclinical safety data

Toxic effects caused by HMG are unknown in humans.

There is no evidence of teratogenic, mutagenic or carcinogenic activity of HMG. Antibodies against HMG can be built up in single cases following repeated cyclical administration of HMG, causing the treatment to be ineffectual.

6.0 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol
Dibasic potassium phosphate
Potassium dihydrogen phosphate

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store between 2°C to 8°C.
Keep the container in the outer carton in order to protect from light.
Do not refrigerate or Freeze.

6.5 Nature and contents of container

Each box of MENOTAS HP 150 contains one Vial of sterile freeze-dried Menotropin 150 IU & one ampoule containing 1 ml of Sodium Chloride Injection (0.9% w/v) BP as solvent.

6.6 Instruction for use / handling

Use immediately after reconstitution.
Discard unused material

7.0 MARKETING AUTHORISATION HOLDER

Intas Pharmaceutical Limited
Corporate House, Near Sola Bridge, S.G. Highway,
Thaltej, Ahmedabad-380054, Gujarat, INDIA

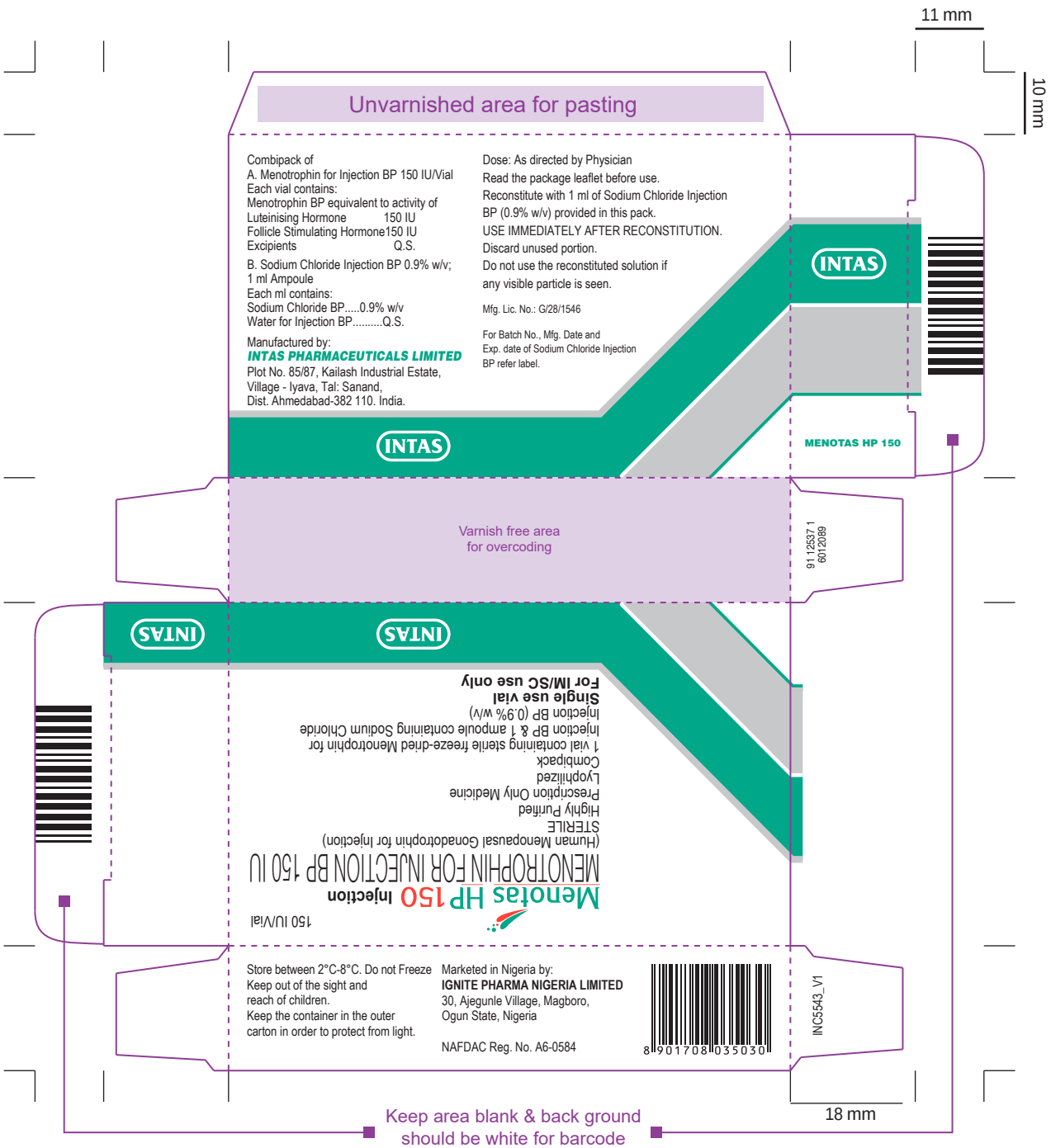
8.0 MARKETING AUTHORISATION NUMBER

A6-0584

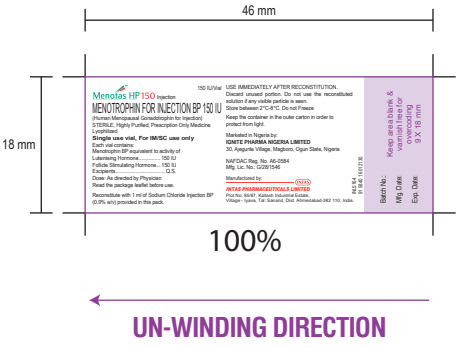
9.0 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
05 June 2020

10.0 DATE OF REVISION OF THE TEXT

June 2020



File Name : 6012089 -MENOTROPHIN 150 IU (-Nig) 1 Vial + 1 Amp BOX
Size : 90 x 20 x 55 mm
Colour : Pantone Green C, Warm Red C & Black
Date : 21*10*21, 30*04*22, 05*05*22



File Name : 6012130 -MENOTROPHIN 150 IU (-Nig) 1 Vial Label
Size : 46 x 18 (mm)
Colour : Pantone Green C, Warm Red C & Black
Date : 21*10*21, 25*03*22, 16*04*22, 10*06*22

PRESCRIBING INFORMATION: For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

MENOTAS HP 150

(MENOTROPHIN FOR INJECTION BP 150 IU)

COMPOSITION

Combipack of

A. Menotrophin For Injection BP 150 IU/vial
Each vial contains:
Menotrophin BP equivalent to activity of
Luteinising Hormone .....150 IU
Follicle Stimulating Hormone.....150 IU
Excipients: Q.S.

B. Sodium Chloride Injection BP 0.9%w/v, 1 ml ampoule
Each ml contains:
Sodium chloride BP.....0.9% w/v
Water for injection BP.....Q.S.

Reconstitute with 1 ml of Sodium Chloride Injection BP (0.9% w/v) provided in this pack.

DESCRIPTION

Menotas HP is a preparation of gonadotropins, extracted from the urine of postmenopausal women. It contains follicle stimulating hormone (FSH) and luteinizing hormone (LH) in a ratio 1:1.

CLINICAL PHARMACOLOGY

Pharmacodynamic properties
Pharmacotherapeutic group: Gonadotrophins
ATC code: G03G A02

Menotrophin (Human Menopausal Gonadotrophin, HMG) is a gonadotrophin extracted from the urine of postmenopausal women. It has both luteinising hormone and follicle stimulating hormone activity in a 1:1 ratio. Human Chorionic Gonadotrophin (hCG), a naturally occurring hormone in postmenopausal urine, is present in MENOTAS HP 150 and is the main contributor of the LH activity.

Menotrophin (HMG) directly affects the ovaries and the testes. HMG has a gametropic and steroidogenic effect.

In the ovaries, the FSH-component in HMG induces an increase in the number of growing follicles and stimulates their development. FSH increases the production of oestradiol in the granulosa cells by aromatising androgens that originate in the Theca cells under the influence of the LH-component.

Follicular growth can be stimulated by FSH in the total absence of LH, but the resulting follicles develop abnormally and are associated with low oestradiol levels and inability to luteinize to a normal ovulatory stimulus.

In line with the action of LH activity in enhancing steroidogenesis, oestradiol levels associated with treatment with MENOTAS HP 150 are higher than with recombinant FSH preparations in downregulated IVF/ICSI cycles. This issue should be considered when monitoring patient's response based on oestradiol levels.

In the testes, FSH induces the transformation of premature to mature Sertoli cells. It mainly causes the maturation of the seminal canals and the development of the spermatozoa. However, a high concentration of androgens within the testes is necessary and can be attained by a prior treatment using hCG.

Pharmacokinetic properties
The pharmacokinetics of menotrophin following intramuscular or subcutaneous administration shows great interindividual variability. After 7 days of repeated dosing with 150 IU MENOTAS HP 150 in downregulated healthy female volunteers, plasma FSH concentrations Cmax (baseline-corrected) (mean ± SD) were 8.9 ± 3.5 IU/L and 8.4 ± 3.2 IU/L for the SC and IM administration, respectively. The area under the curve (AUC) of FSH concentration was (mean ± SD) 180 ± 77 h.IU/L and 166 ± 67 h.IU/L for SC and IM administration, respectively. Maximum FSH concentrations were reached (Tmax) within 7 hours for both routes of administration. After repeated administration, FSH was eliminated with a halflife (T1/2) (mean ± SD) of 30 ± 11 hours and 27 ± 9 hours for the SC and IM administration, respectively. Although the individual LH concentration versus time curves show an increase in the LH concentration after dosing with MENOTAS HP 150, the data available were too sparse to be subjected to a pharmacokinetic analysis.

Menotrophin is excreted primarily via the kidneys.
The pharmacokinetics of MENOTAS HP 150 in patients with renal or hepatic impairment has not been investigated.

INDICATIONS

Treatment of female and male infertility in the following groups of patients:

Anovulation, including polycystic ovarian disease (PCOD) in women who have been unresponsive to treatment with clomiphene citrate:

- Women undergoing controlled ovarian hyperstimulation: MENOTAS HP 150 can induce the development of multiple follicles for assisted reproductive technologies (ART) (e.g. in vitro fertilisation/embryo transfer (IVF/ET), gamete intra-fallopian transfer (GIFT) and intracytoplasmic sperm injection (ICSI)).
- Hypogonadotrophic hypogonadism in men: MENOTAS HP 150 may be given in combination with human chorionic gonadotrophin (e.g. Choragon) for the stimulation of spermatogenesis. Patients with primary testicular failure are usually unresponsive

DOSAGE AND ADMINISTRATION

Treatment with MENOTAS HP 150 should be initiated under the supervision of a physician experienced in the treatment of fertility problems.

Posology
For intramuscular or subcutaneous use. The dosage regimens described below are identical for both forms of administration.

There are great inter-individual variations in the response of the ovaries to exogenous gonadotrophins. This makes it impossible to set a uniform dosage scheme. The dosage should, therefore, be adjusted individually depending on the ovarian response. Recommendations about dosage and duration of treatment may change depending on the actual treatment protocol.

Anovulatory infertility:
Menotrophin is administered to induce follicular maturation and is followed by treatment with chorionic gonadotrophin to stimulate ovulation and corpus luteum formation.

MENOTAS HP 150 therapy should start within the initial 7 days of the menstrual cycle. The recommended initial dose of MENOTAS HP 150 is 75-150 IU daily, which should be maintained for at least 7 days. Based on clinical monitoring (including ovarian ultrasound alone or in combination with measurement of oestradiol levels) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than every 7 days. The recommended dose increment is 37.5 IU per adjustment and should not exceed 75 IU. The maximum daily dose should not be higher than 225 IU. If a patient fails to respond adequately after 3 weeks of treatment, that cycle should be abandoned, and the patient should recommence treatment at a higher starting dose than in the abandoned cycle.

When an optimal response is obtained, administration of MENOTAS HP 150 is stopped. A single injection of 5,000 IU to 10,000 IU of hCG should be given 1 day after the last MENOTAS HP 150 injection. The patient is recommended to have coitus on the day of and the day following hCG administration. Alternatively, intrauterine insemination (IUI) may be performed. If an excessive response to MENOTAS HP 150 is obtained, treatment should be stopped and hCG withheld, and the patient should use a barrier method of contraception or refrain from having coitus until the next menstrual bleeding has started. Treatment should recommence in the next treatment cycle at a dose lower than in the previous cycle.

Women undergoing controlled ovarian hyperstimulation for multiple follicular development for assisted reproductive technologies (ART):
In a protocol using down-regulation with a GnRH agonist, MENOTAS HP 150 therapy should start approximately 2 weeks after the start of agonist treatment. In a protocol using down-regulation with a GnRH antagonist, MENOTAS HP 150 therapy should start on day 2 or 3 of the menstrual cycle. The recommended initial dose of MENOTAS HP 150 is 150-225 IU daily for at least the first 5 days of treatment. Based on clinical monitoring (including ovarian ultrasound alone or in combination with measurement of oestradiol levels) subsequent dosing should be adjusted according to individual patient response and should not exceed more than 150 IU per adjustment. The maximum daily dose given should not be higher than 450 IU daily and, in most cases, dosing beyond 20 days is not recommended.

When a suitable number of follicles have reached an appropriate size a single injection of 5,000 IU up to 10,000 IU hCG should be administered to induce final follicular maturation in preparation for oocyte retrieval. Patients should be followed closely for at least 2 weeks after hCG administration. If an excessive response to MENOTAS HP 150 is obtained treatment should be stopped and hCG withheld and the patient should use a barrier method of contraception or refrain from having coitus until the next menstrual bleeding has started.

Male infertility:
Spermatogenesis is stimulated with chorionic gonadotrophin (1000 – 2000 IU two to three times a week) and then menotrophin is given in a dose of 75 or 150 IU units of FSH with 75 or 150 IU units of LH two or three times weekly. Treatment should be continued for at least 3 or 4 months.

Paediatric population:
There is no relevant use of MENOTAS HP 150 in the paediatric population.

Elderly:
There is no relevant use of MENOTAS HP 150 in the elderly population.

Method of Administration:
By intramuscular or subcutaneous use.
The powder must be reconstituted immediately with the solvent provided prior to use. In order to avoid the injection of large volumes up to 3 vials of the powder may be dissolved in 1 ml of the solvent provided.

Shaking should be avoided. The solution should not be used if it contains particles or if it is not clear.

CONTRAINDICATIONS

Women and Men
MENOTAS HP 150 is contraindicated in women and men with:
- Tumours of the pituitary gland or hypothalamus
- Hypersensitivity to the active substance or to any of the excipients

Women
- Ovarian, uterine or mammary carcinoma
- Pregnancy and lactation
- Gynaecological haemorrhage of unknown aetiology
- Ovarian cysts or enlarged ovaries not due to polycystic ovarian disease.

In the following situations treatment outcome is unlikely to be favourable, and therefore MENOTAS HP 150 should not be administered:
- Primary ovarian failure
- Malformation of sexual organs incompatible with pregnancy
- Fibroid tumours of the uterus incompatible with pregnancy
- Structural abnormalities in which a satisfactory outcome cannot be expected, for example, tubal occlusion (unless superovulation is to be induced for IVF), ovarian dysgenesis, absent uterus or premature menopause.

Men
- Tumours in the testes
- Prostate carcinoma

SPECIAL WARNINGS AND PRECAUTIONS

MENOTAS HP 150 is a potent gonadotropic substance capable of causing mild to severe adverse reactions and should only be used by physicians who are thoroughly familiar with infertility problems and their management.

Gonadotrophin therapy requires a certain time commitment by physicians and supportive health professionals, and calls for monitoring of ovarian response with ultrasound, alone or in combination with measurement of serum oestradiol levels, on a regular basis. There is considerable inter-patient variability in response to menotrophin administration, with a poor response to menotrophin in some patients. The lowest effective dose in relation to the treatment objective should be used.

The first injection of MENOTAS HP 150 should be performed under direct medical supervision.

Before starting treatment, the couple's infertility should be assessed as appropriate and putative contraindications for pregnancy evaluated. In particular, patients should be evaluated for hypothyroidism, adrenocortical deficiency, hyperprolactinemia and pituitary or hypothalamic tumours, and appropriate specific treatment given.

Patients undergoing stimulation of follicular growth, whether in the frame of a treatment for anovulatory infertility or ART procedures may experience ovarian enlargement or develop hyperstimulation. Adherence to recommended MENOTAS HP 150 dosage and regimen of administration, and careful monitoring of therapy will minimise the incidence of such events.

Acute interpretation of the indices of follicle development and maturation requires a physician who is experienced in the interpretation of the relevant tests.

Ovarian Hyperstimulation Syndrome (OHSS)
OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS is a syndrome that can manifest itself with increasing degrees of severity. It comprises marked ovarian enlargement, high serum sex steroids, and an increase in vascular permeability which can result in an accumulation of fluid in the peritoneal, pleural and rarely, in the pericardial cavities.

The following symptoms may be observed in cases of OHSS: abdominal pain, abdominal distension, severe ovarian enlargement, weight gain, dyspnoea, oliguria and gastrointestinal symptoms including nausea, vomiting and diarrhoea.

Clinical evaluation may reveal hypovolaemia, haemoconcentration, electrolyte imbalances, ascites, haemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events.

If urinary oestrogen levels exceed 540 nmol (150 micrograms)/24 hours, or if plasma 17 beta-oestradiol levels exceed 3000 pmol/L (800 picograms/ml), or if there is any steep rise in values, there is an increased risk of hyperstimulation and MENOTAS HP 150 treatment should be immediately discontinued and human chorionic gonadotrophin withheld. Ultrasound will reveal any excessive follicular development and unintentional hyperstimulation.

The severe form OHSS may be life-threatening and is characterised by large ovarian cysts (prone to rupture), acute abdominal pain, ascites, very often hydrothorax and occasionally thromboembolic phenomena. Other symptoms that may be observed include: abdominal distension, severe ovarian enlargement, weight gain, dyspnoea, oliguria and gastrointestinal symptoms including nausea, vomiting and diarrhoea. Clinical evaluation may reveal hypovolaemia, haemoconcentration, electrolyte imbalances, haemoperitoneum, pleural effusions and acute pulmonary distress.

Excessive ovarian response to gonadotrophin treatment seldom gives rise to OHSS unless hCG is administered to trigger ovulation. Therefore, in cases of ovarian hyperstimulation it is prudent to withhold hCG and advise the patient to refrain from coitus or to use barrier methods for at least 4 days. OHSS may progress rapidly (within 24 hours to several days) to become a serious medical event, therefore patients should be followed for at least two weeks after the hCG administration.

Adherence to recommended MENOTAS HP 150 dosage, regimen of administration and careful monitoring of therapy will minimise the incidence of ovarian hyperstimulation and multiple pregnancy. Patients undergoing controlled ovarian hyperstimulation may be at an increased risk of developing hyperstimulation in view of the excessive oestrogen response and multiple follicular development. In ART, aspiration of all follicles prior to ovulation may reduce the occurrence of hyperstimulation.

OHSS may be more severe and more protracted if pregnancy occurs. Most often, OHSS occurs after hormonal treatment has been discontinued and reaches its maximum severity at about seven to ten days following treatment. Usually, OHSS resolves spontaneously with the onset of menses.

If severe OHSS occurs, gonadotrophin treatment should be stopped if still ongoing, the patient hospitalised and specific therapy for OHSS started.

This syndrome occurs with higher incidence in patients with polycystic ovarian disease.

Multiple pregnancy
Multiple pregnancy, especially high order, carries an increased risk of adverse maternal and perinatal outcomes.

In patients undergoing ovulation induction with gonadotrophins, the incidence of multiple pregnancies is increased compared with natural conception. The majority of multiple conceptions are twins. To minimise the risk of multiple pregnancy, careful monitoring of ovarian response is recommended.

In patients undergoing ART procedures the risk of multiple pregnancy is related mainly to the number of embryos replaced, their quality and the age of the patient.

The patient should be advised of the potential risk of multiple births before starting treatment.

Pregnancy wastage
The incidence of pregnancy wastage by miscarriage or abortion is higher in patients undergoing stimulation of follicular growth for ART procedures than in the normal population.

Ectopic pregnancy
Women with a history of tubal disease are at risk of ectopic pregnancy, whether the pregnancy is obtained by spontaneous conception or with fertility treatment. The prevalence of ectopic pregnancy after IVF has been reported to be 2 to 5%, as compared to 1 to 1.5% in the general population.

Reproductive system neoplasms
There have been reports of ovarian and other reproductive system neoplasms, both benign and malignant, in women who have undergone multiple drug regimens for infertility treatment. It is not yet established if treatment with gonadotrophins increases the baseline risk of these tumours in infertile women.

Congenital malformation
The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies.

Thromboembolic events
Women with generally recognised risk factors for thromboembolic events, such as personal or family history, severe obesity (Body Mass Index > 30kg/m2) or thrombophilia may have an increased risk of venous or arterial thromboembolic events, during or following treatment with gonadotrophins. In these women, the benefits of gonadotrophin administration need to be weighed against the risks. It should be noted however, that pregnancy itself also carries an increased risk of thromboembolic events.

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed with MENOTAS HP 150 in humans.

Although there is no controlled clinical experience, it is expected that the concomitant use of MENOTAS HP 150 and clomiphene citrate may enhance the follicular response. When using GnRH agonist for pituitary desensitization, a higher dose of MENOTAS HP 150 may be necessary to achieve adequate follicular response.

FERTILITY, PREGNANCY AND LACTATION

Fertility
MENOTAS HP 150 is indicated for use in infertility.

Pregnancy
MENOTAS HP 150 is contraindicated in women who are pregnant.
There are no or limited amount of data from the use of menotrophins in pregnant women. No animal studies have been carried out to evaluate the effects of MENOTAS HP 150 during pregnancy.

Breast-feeding
MENOTAS HP 150 is contraindicated in women who are breast-feeding.

UNDESIRABLE EFFECTS

The most frequently reported adverse drug reactions (ADR) during treatment with MENOTAS HP 150 in clinical trials are Ovarian Hyperstimulation Syndrome OHSS, abdominal pain, headache, abdominal distension, and injection site pain. None of these ADRs have been reported with an incidence rate of more than 5%.

The table below displays the main ADR in women treated with MENOTAS HP 150 in clinical trials distributed by system organ classes (SOCs) and frequency. ADRs seen during post-marketing experience are mentioned with unknown frequency.

System Organ Class	Common (> 1/100 to < 1/10)	Uncommon (> 1/1,000 to < 1/100)	Rare (> 1/10,000 to < 1/1,000)	Unknown
Eye disorders				Visual disorders
Gastrointestinal disorders	Abdominal pain, Abdominal distension, Nausea	Vomiting, Abdominal discomfort, Diarrhoea		
General disorders and administration site condition	Injection site reactions [a]	Fatigue		
Immune system disorders				Hypersensitivity reactions [b]
Investigations				
Musculoskeletal & connective tissue disorders				Musculoskeletal pain [c]
Nervous system disorders	Headache	Dizziness		
Reproductive system disorders	OHSS [d], Pelvic pain[e]	Ovarian cyst, Breast complaints [f]		Ovarian torsion [d]
Skin and subcutaneous tissue disorders			Acne, Rash	Pruritus, Urticaria
Vascular Disorders		Hot flush		

a Most frequently reported injection site reaction was injection site pain.
b Cases of localised or generalised allergic reactions, including anaphylactic reaction, along with associated symptomatology have been reported rarely.
c Musculoskeletal pain includes arthralgia, back pain, neck pain and pain in extremities.
d Gastrointestinal symptoms associated with OHSS such as abdominal distension and discomfort, nausea, vomiting, diarrhoea have been reported with MENOTAS HP 150 in clinical trials. In cases of severe OHSS ascites and pelvic fluid collection, pleural effusion, dyspnoea, oliguria, thromboembolic events and ovarian torsion have been reported as rare complications.
e Pelvic pain includes ovarian pain and adnexa uteri pain.
f Breast complaints include breast pain, breast tenderness, breast discomfort, nipple pain and breast swelling.

OVERDOSE

The effects of an overdose is unknown, nevertheless one could expect ovarian hyperstimulation syndrome to occur.

STORAGE

Store between 2°C-8°C. Do not Freeze.
Keep the container in the outer carton in order to protect from light.

To be used immediately after reconstitution. Discard unused material

PRESENTATION

Each box of MENOTAS HP 150 contains one Vial of sterile freeze-dried Menotrophin 150 IU & one ampoule containing 1 ml of Sodium Chloride Injection (0.9% w/v) BP as solvent.

Manufactured by
INTAS
INTAS PHARMACEUTICALS LTD.
Plot No. 85/87, Kailash Industrial
Estate,Village-Iyava, Tal: Sanand,
Dist: Ahmedabad-382 110, India.

Marketed in Nigeria by:
IGNITE PHARMA NIGERIA LIMITED
30, Ajegunle Village, Magboro,
Ogun State, Nigeria
NAFDAC Reg. No. A6-0584

Front Side

Back Side

File Name : 6011987 -MENOTROPHIN 150 IU (-Nig) Multiple PackStyle PIL
Size : 170 x 550 mm (Front/Back side) (Text area 145 x 540 mm)
Colour : Black
Date : 21*10*21, 21*02*22, 25*03*22, 16*04*22, 10*06*22