SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MENOPUR 600 IU solution for injection in pre-filled pen

MENOPUR 1200 IU solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MENOPUR 600 IU solution for injection:
One pre-filled multidose pen delivers highly purified menotrophin (human menopausal gonadotrophin, HMG) corresponding to follicle stimulating hormone activity FSH 600 IU and luteinizing hormone activity LH 600 IU in 0.96 mL solution.

MENOPUR 1200 IU solution for injection:
One pre-filled multidose pen delivers highly purified menotrophin (human menopausal gonadotrophin, HMG) corresponding to follicle stimulating hormone activity FSH 1200 IU and luteinizing hormone activity LH 1200 IU in 1.92 mL solution.

One mL of solution contains 625 IU FSH activity and 625 IU LH activity.

Human Chorionic Gonadotrophin (hCG), a naturally occurring hormone in postmenopausal urine, is present in MENOPUR and is the main contributor of the LH activity.

The active ingredient in MENOPUR is obtained from the urine of postmenopausal women.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled pen (injection).

Clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MENOPUR is indicated for the treatment of infertility in the following clinical situations:

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) (e.g. in vitro fertilisation/embryo transfer (IVF/ET), gamete intra-fallopian transfer (GIFT) and intracytoplasmic sperm injection (ICSI)).

4.2 Posology and method of administration

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

Posology

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. MENOPUR can be given alone or in combination with a gonadotrophin-releasing hormone (GnRH) agonist or antagonist. Recommendations about dosage and duration of treatment may change depending on the actual treatment protocol.

Women with anovulation (including PCOD)

The object of MENOPUR therapy is to develop a single Graafian follicle from which the oocyte will be liberated after the administration of human chorionic gonadotrophin (hCG).

MENOPUR therapy should start within the initial 7 days of the menstrual cycle. The recommended initial dose of MENOPUR 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 4 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, a single injection of 5,000 IU to 10,000 IU hCG should be given 1 day after the last MENOPUR 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 MENOPUR is obtained treatment should be stopped and hCG withheld (see section 4.4) and the patient should use a barrier method of contraception or refrain from having coitus until the next menstrual bleeding has started.

Women undergoing controlled ovarian hyperstimulation for multiple follicular development for assisted reproductive technologies (ART)

In a protocol using down-regulation with a GnRH agonist, MENOPUR therapy should start approximately 2 weeks after the start of the agonist treatment. In a protocol using down-regulation with a GnRH antagonist, MENOPUR therapy should start on day 2 or 3 of the menstrual cycle. The recommended initial dose of MENOPUR 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 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 MENOPUR is obtained treatment should be stopped and hCG withheld (see section 4.4) and the patient should use a barrier method of contraception or refrain from having coitus until the next menstrual bleeding has started.

Renal/hepatic impairment

Patients with renal and hepatic impairment have not been included in clinical trials (see section 5.2).

Paediatric population

There is no relevant use of MENOPUR in the paediatric population.

Method of administration

MENOPUR is intended for subcutaneous (S.C.) injection, preferably in the abdominal wall. The first injection should be performed under direct medical supervision. Patients must be educated on how to

use the MENOPUR injection pen and to perform injections. Self-administration should only be performed by patients who are well motivated, adequately trained and have access to expert advice.

For instructions on the administration with the pre-filled pen, see the "Instructions for Use" supplied in the package with the pen.

4.3 Contraindications

MENOPUR is contraindicated in women who have:
- Tumours of the pituitary gland or hypothalamus
- Ovarian, uterine or mammary carcinoma
- Pregnancy and lactation
- Gynaecological haemorrhage of unknown aetiology
- Hypersensitivity to the active substance or any of the excipients listed in section 6.1
- Ovarian cysts or enlarged ovaries not due to polycystic ovarian disease.

In the following situations treatment outcome is unlikely to be favourable, and therefore MENOPUR should not be administered:
- Primary ovarian failure
- Malformation of sexual organs incompatible with pregnancy
- Fibroid tumours of the uterus incompatible with pregnancy

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

MENOPUR is a potent gonadotrophic 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 preferably 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.

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 MENOPUR 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 severe 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.

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 MENOPUR dosage, regimen of administration and careful monitoring of therapy will minimise the incidence of ovarian hyperstimulation and multiple pregnancy (see sections 4.2 and 4.8). 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 tumors 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 >30 kg/m^2) 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.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with MENOPUR in humans.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
MENOPUR is contraindicated in women who are pregnant (see section 4.3).
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 MENOPUR during pregnancy (see section 5.3).

Breastfeeding
MENOPUR is contraindicated in women who are lactating (see section 4.3).

Fertility
MENOPUR is indicated for use in infertility (see section 4.1).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, MENOPUR is unlikely to have influence on the patient's ability to drive and use machines.

4.8 Undesirable effects

The most serious and frequently reported adverse drug reactions reported during treatment with MENOPUR in clinical trials are OHSS, abdominal pain, headache, abdominal distension and injection site pain, with an incidence rate up to 5%. The table below displays the main adverse drug reactions in women treated with MENOPUR in clinical trials distributed by system organ classes (SOCs) and frequency. Further, the ADRs seen during post-marketing experience are mentioned with unknown frequency.

System Organ Class	**Common (≥ 1/100 to < 1/10)**	**Uncommon (≥ 1/1000 to < 1/100)**	**Rare (≥ 1/10,000 to < 1/1,000)**	**Unknown**
Eye disorders				Visual disorders [a]
Gastrointestinal disorders	Abdominal pain, Abdominal distension, nausea, enlarged abdomen	Vomiting, Abdominal discomfort, Diarrhoea		

General disorders and administration site condition	Injection site reactions [b]	Fatigue		Pyrexia, Malaise
Immune system disorders				Hypersensitivity reactions [c]
Investigations				Weight increased
Musculoskeletal & connective tissue disorders				Musculoskeletal pain [d]
Nervous system disorders	Headache	Dizziness		
Reproductive system disorders	OHSS [e], pelvic pain [f]	Ovarian cyst, Breast complaints [g]		Ovarian torsion [e]
Skin and subcutaneous tissue disorders			Acne, Rash	Pruritus, Urticaria
Vascular disorders		Hot flush		Thromboembolism [e]

[a] Individual cases of temporary amaurosis, diplopia, mydriasis, scotoma, photopsia, vitreous floaters, vision blurred and vision impairment have been reported as visual disorders during the post-marketing period.

[b] Most frequently reported injection site reaction was injection site pain.

[c] Cases of localised or generalised allergic reactions, including anaphylactic reaction, along with associated symptomatology have been reported rarely.

[d] Musculoskeletal pain includes arthralgia, back pain, neck pain and pain in extremities.

[e] Gastrointestinal symptoms associated with OHSS such as abdominal distension and discomfort, nausea, vomiting and diarrhoea have been reported with MENOPUR 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.

[f] Pelvic pain includes ovarian pain and adnexa uteri pain.

[g] Breast complaints include breast pain, breast tenderness, breast discomfort, nipple pain and breast swelling.

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 <the national reporting system> <[to be completed nationally]>

4.9 Overdose

The effect of an overdose is unknown, nevertheless one could expect ovarian hyperstimulation syndrome to occur (see section 4.4).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gonadotrophins, ATC code: G03G A02

MENOPUR is produced from the urine of postmenopausal women. Human Chorionic Gonadotrophin (hCG), a naturally occurring hormone in postmenopausal urine, is present in MENOPUR and is the main contributor of the LH activity.

Menotrophin, which contains both FSH and LH activity, induces ovarian follicular growth and development as well as gonadal steroid production in women who do not have primary ovarian failure. FSH is the primary driver of follicular recruitment and growth in early folliculogenesis, while LH is important for ovarian steroidogenesis and is involved in the physiological events leading to the development of a competent pre-ovulatory follicle. 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 stereoidogenesis, oestradiol levels associated with treatment with MENOPUR 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. The difference in oestradiol levels is not found when using low-dose ovulation induction protocols in anovulatory patients.

5.2 Pharmacokinetic properties

The pharmacokinetic profile of the FSH in MENOPUR has been documented. After 7 days of repeated dosing with 150 IU MENOPUR in downregulated healthy female volunteers, maximum plasma FSH concentrations (baseline-corrected) (mean ± SD) were 8.9 ± 3.5 IU/L and 8.5 ± 3.2 IU/L for the SC and IM administration, respectively. Maximum FSH concentrations were reached within 7 hours for both routes of administration. After repeated administration, FSH was eliminated with a half-life (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 MENOPUR, the data available were too sparse to be subjected to a pharmacokinetic analysis.

Menotrophin is excreted primarily via the kidneys.

The pharmacokinetics of MENOPUR in patients with renal or hepatic impairment has not been investigated.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans, which is not known from the extensive clinical experience. Reproduction toxicity studies have not been carried out to evaluate the effects of MENOPUR during pregnancy or postpartum as MENOPUR is not indicated during these periods.
MENOPUR consist of naturally occurring hormones and should be expected to be non-genotoxic. Carcinogenicity studies have not been carried out as the indication is for short term treatment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Methionine
Arginine hydrochloride
Polysorbate 20
Sodium hydroxide

Hydrochloric acid
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years

In-Use: 28 days.
Store below 25 °C when in-use.

In-use stability has been demonstrated for 28 days at 25°C. Therefore, once opened, the product may be stored for a maximum of 28 days below 25°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.

Always store the pen with the pen cap on, in order to protect from light.

For storage conditions after first use of the medicinal product, see section 6.3.

6.5 Nature and contents of container

MENOPUR 600 IU solution for injection:
Multidose cartridge (Type I glass) with a plunger (rubber) and a crimp cap (aluminium) with bi-layer septum (rubber). Each cartridge contains 0.96 mL of solution.
Pack size of 1 pre-filled pen and 12 injection needles (stainless steel).

MENOPUR 1200 IU solution for injection:
Multidose cartridge (Type I glass) with a plunger (rubber) and a crimp cap (aluminium) with bi-layer septum (rubber). Each cartridge contains 1.92 mL of solution.
Pack size of 1 pre-filled pen and 21 injection needles (stainless steel).

6.6 Special precautions for disposal

The solution should not be administered if it contains particles or is not clear.

The instructions for use of the pen must be followed. Discard used needles immediately after injection.

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

7. MARKETING AUTHORISATION HOLDER

Local Ferring Company
<[To be completed nationally]>

{Name and address}
<{tel}>

<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

Local MA number
<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>

<[To be completed nationally]>

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

MENOPUR 600 IU solution for injection in a pre-filled pen
menotrophin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled multidose pen delivers 600 IU menotrophin (HMG) corresponding to FSH 600 IU activity and LH 600 IU activity.
One mL of solution contains 625 IU FSH activity and 625 IU LH activity.

3. LIST OF EXCIPIENTS

Excipients: phenol, methionine, arginine hydrochloride, polysorbate 20, sodium hydroxide, hydrochloric acid, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen
1 multidose pre-filled pen with 12 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
For multiple injections.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store the pen in a refrigerator at 2°C to 8°C. Do not freeze.

After opening: Use the pen within 28 days of opening. Store below 25°C.
Always store the pen with the pen cap on, in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

{Name and Address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MENOPUR 600 IU solution for injection in pre-filled pen

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

MENOPUR 600 IU solution for injection
menotrophin
Subcutaneous use.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP
After first use: Use within 28 days. Store below 25 °C.

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

600 IU

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

MENOPUR 1200 IU solution for injection in a pre-filled pen
menotrophin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled multidose pen delivers 1200 IU menotrophin (HMG) corresponding to FSH 1200 IU activity and LH 1200 IU activity.
One mL of solution contains 625 IU FSH activity and 625 IU LH activity.

3. LIST OF EXCIPIENTS

Excipients: phenol, methionine, arginine hydrochloride, polysorbate 20, sodium hydroxide, hydrochloric acid, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled pen
1 multidose pre-filled pen with 21 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.
For multiple injections.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Before use:
Store the pen in a refrigerator at 2°C to 8°C. Do not freeze.

After opening: Use the pen within 28 days of opening. Store below 25°C.
Always store the pen with the pen cap on, in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

{Name and Address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MENOPUR 1200 IU solution for injection in pre-filled pen

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

MENOPUR 1200 IU solution for injection
menotrophin
Subcutaneous use.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP
After first use: Use within 28 days. Store below 25 °C.

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1200 IU

6. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the user

MENOPUR 600 IU solution for injection in pre-filled pen

MENOPUR 1200 IU solution for injection in pre-filled pen

menotrophin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What MENOPUR is and what it is used for

MENOPUR comes as a solution for injection in a pre-filled pen. The injection is given under your skin ('sub-cutaneous' injection) – usually in the tummy.

MENOPUR contains 'menotrophin', which is a mixture of two natural hormones called:
- follicle stimulating hormone (FSH) and
- luteinizing hormone (LH).

These hormones help reproductive organs to work normally. The FSH and LH hormones in menotrophin are obtained from the urine of women who have passed the menopause.

What MENOPUR is used for

MENOPUR is used to treat women who cannot become pregnant. It is used for:
- women whose ovaries do not produce eggs. This includes women with 'polycystic ovarian disease' ('PCOD'). MENOPUR is used when women have already had a medicine called 'clomiphene citrate', but this medicine has not helped.
- women in 'assisted reproductive technology' programmes. This includes:
  - o 'In vitro fertilisation' (IVF) or 'embryo transfer' (ET)
  - o 'Gamete intra-fallopian transfer' (GIFT)
  - o 'Intracytoplasmic sperm injection' (ICSI).

How MENOPUR works

MENOPUR helps the ovaries to develop lots of egg sacs ('follicles') where an egg might develop. This is called 'multiple follicular development'.

2. What you need to know before you use MENOPUR

Checks before you use MENOPUR
Before you use MENOPUR, you and your partner should be checked by a doctor for the causes of your fertility problems. In particular, you should be checked for the following so that another more suitable treatment can be given:
- Under-active thyroid or adrenal glands
- High levels of a hormone called prolactin – called 'hyperprolactinemia'
- Tumours of the 'pituitary gland' – this is at the base of the brain
- Tumours of the 'hypothalamus' (under the part of the brain called the 'thalamus').

If you have any of the conditions listed above, **please tell your doctor before starting treatment with MENOPUR.**

Do not use MENOPUR if:
- you are allergic to menotrophin or any of the other ingredients of MENOPUR (listed in Section 6)
- you have cancer of the womb ('uterus'), ovaries, breasts, or parts of the brain such as the pituitary
- gland or hypothalamus
- you have sacs of fluid on your ovaries ('ovarian cysts') or enlarged ovaries – unless your enlarged
- ovaries are caused by PCOD
- you have any physical problems with the womb or other sexual organs
- you have bleeding from the vagina for an unknown reason
- you have fibroids – these are tumours in your womb that are not cancer
- you are pregnant or breast-feeding

Warnings and precautions

Ovarian Hyperstimulation Syndrome (OHSS)
A serious side effect of this medicine, especially in women with PCOD, is 'ovarian hyperstimulation syndrome' or 'OHSS' (see Section 4).

Tell your doctor straight away if you have signs of
OHSS, even if:
- some days have passed after your last injection
- you stop using MENOPUR.

These can be signs of high levels of activity in the ovaries, which might become severe. If this happens, your doctor will stop your MENOPUR treatment and you will be treated in a hospital.

Keeping to your recommended dose, and careful monitoring of your treatment, will reduce your chances of getting these symptoms.

Scans and tests
While you are being treated with this medicine, your doctor will normally arrange for you to have **ultrasound scans** and sometimes **blood tests** to check your response to treatment.

Pregnancy risks
Being treated with hormones like MENOPUR can increase the risk of:
- pregnancy outside of the womb (ectopic pregnancy) if you have ever had fallopian tube disease
- miscarriage
- multiple pregnancy (for example twins or triplets)
- physical defects in the baby at birth (congenital malformations).

Some women who have been given infertility treatment with more than one medicine have developed tumours in the ovaries and in other reproductive organs. It is not yet known if treatment with hormones like MENOPUR causes these problems.

Blood clots
Blood clots are more likely to form inside your blood vessels when you are pregnant. This is more likely if you have had treatment to help you become pregnant and:
- you are overweight

- you have a blood clotting disease ‘thrombophilia’
- you or someone in your family has had blood clots.

Tell your doctor if you think this applies to you.

Children
MENOPUR is not used in children.

Other medicines and MENOPUR
Tell your doctor if you are taking, have recently taken, or might take any other medicines.

Clomiphene citrate is another medicine used in the treatment of infertility. If MENOPUR is used at the same time as clomiphene citrate, the effect on the ovaries may be increased.

Pregnancy and breast-feeding
Do not use MENOPUR if you are pregnant or breast-feeding.

Driving and using machines
MENOPUR is unlikely to affect your ability to drive and use machines.

Important information about some of the ingredients of MENOPUR
MENOPUR contains less than 1 mmol sodium (23 mg) per dose, so it is essentially ‘sodium-free’.

3. How to use MENOPUR

Always use MENOPUR exactly as your doctor has told you. You should check with your doctor if you are not sure.

Women who are not producing eggs (not ovulating):
Your treatment will start within the first 7 days of your menstrual cycle.
- Day 1 is the first day of your period.
- You will have injections every day for at least 7 days.

<u>How much MENOPUR?</u>
The normal starting dose is between 75 and 150 IU every day.
- The dose may be adjusted depending on your response – up to 225 IU.
- You will have the chosen dose for at least 7 days before the doctor changes it.
- The dose will normally be increased by 37.5 IU at a time. It will not be increased by more than 75 IU each time.

Your doctor will monitor the effect of MENOPUR treatment. The treatment cycle will stop if you do not respond to the treatment after 4 weeks.

<u>If you have a good response to MENOPUR:</u>
You will get a single injection of a hormone called ‘human chorionic gonadotrophin’ (hCG).
- The dose will be between 5,000 and 10,000 IU
- You will get the hCG injection one day after your last MENOPUR injection.

You should have sex on the day of the hCG injection **and** the day after. Alternatively, sperm may be injected directly into your womb, known as ‘artificial insemination’
- Your doctor will then monitor you closely for at least two weeks.

<u>If you do not respond to MENOPUR:</u>
- Your doctor will monitor the effect of MENOPUR treatment
- Depending on your progress, your doctor may decide to stop treatment with MENOPUR and not give you the hCG injection

Women in assisted reproduction programmes:
If you are in an assisted reproduction programme, you will also have a medicine which helps a hormone called 'Gonadotropin Releasing Hormone' (GnRH) to work. This other medicine is called a 'GnRH agonist'. MENOPUR should be started around 2 weeks after the start of the GnRH agonist therapy.

You may also be having a medicine called a 'GnRH antagonist'.

MENOPUR treatment should be started on day 2 or 3 of the menstrual cycle (day 1 is the first day of your period).

How much MENOPUR?
MENOPUR should be given every day for at least 5 days.
- The initial dose of MENOPUR is normally 150–225 IU.
- This dose may be increased according to your response to the treatment – up to a maximum of 450 IU per day.
- The dose should not be increased by more than 150 IU each time.

Normally, treatment should not continue for more than 20 days.

If enough egg sacs (or follicles) are present, you will be given a single injection of hCG at a dose of up to 10,000 IU to cause the release of an egg (ovulation).

Your doctor will closely monitor your progress for at least 2 weeks after you have been given the hCG injection.

Your doctor will monitor the effect of MENOPUR treatment.
- Depending on your progress, your doctor may decide to stop treatment with MENOPUR and not give you the hCG injection.
- In this case, you will be told to use a barrier method of contraception (for example a condom).

Otherwise you should not have sexual intercourse until your next period has started.

Using MENOPUR
Follow the 'Instructions for Use', supplied in the package with the pre-filled pen, very carefully.

A doctor or nurse will be there for your first injection of MENOPUR. Your doctor will decide if you can give yourself the following injections at home – after you have been fully trained.

You will be given MENOPUR as an injection under the skin ('sub-cutaneous' injection). This is usually in the tummy. Each pre-filled pen may be used for several injections.

If you take more MENOPUR than you should
Tell your doctor.

If you forget to take MENOPUR
Do not take a double dose to make up for a forgotten dose. Tell your doctor.

4. Possible side effects

Like all medicines, MENOPUR can cause side effects, although not everybody gets them.

Serious side effects

Ovarian Hyperstimulation Syndrome (OHSS)
Tell your doctor straight away if you experience any of the following, which may be signs of OHSS:
- you have pain or swelling of the tummy
- you feel or are sick

- you have diarrhoea
- you put on weight
- you have difficulty breathing
- you need to pass water less often.

Tell your doctor straight away, even if a few days have passed since your last injection, or you stop using MENOPUR. You may need urgent medical treatment. These side effects may mean that your ovaries have been stimulated too much, known as Ovarian Hyperstimulation Syndrome (OHSS). In cases of severe OHSS, build-up of fluid in the tummy, pelvis or chest cavity, difficulty in breathing, decreased urination, formation of blood clots in blood vessels (thromboembolism) and twisting of ovaries (ovarian torsion) have been reported as rare complications.

Allergic reactions
Tell your doctor straight away if you have:
- rash
- itching
- swelling of the throat and difficulty breathing.

If you notice any of the above signs, tell your doctor straight away.

Other side effects

Common side effects (may affect up to 1 in 10 people):
- Headache
- Feeling sick (nausea)
- Pain or swelling of the tummy
- Pelvic pain
- Pain, redness, swelling, itching or bruising where the injection was given.

Uncommon side effects (may affect up to 1 in 100 people):
- Being sick (vomiting)
- Pain in the tummy
- Diarrhoea
- Feeling tired (fatigue)
- Feeling dizzy
- Sacs of fluid within ovaries (ovarian cysts)
- Breast problems, such as pain, tenderness, discomfort, swelling or nipple pain
- Hot flushes.

Very rare side effects (may affect up to 1 in 1,000 people):
- Spots (acne).

Other side effects (it is not known yet how many people they may affect):
- Problems with eyesight
- Fever
- Feeling generally unwell
- Increase in weight
- Muscle and joint pains
- Twisting of the ovary (ovarian torsion) because of overstimulation
- Hives
- Blood clots because the ovaries have been overstimulated.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via <the national reporting system> <[to be completed nationally]>. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store MENOPUR

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the pre-filled pen label and carton after 'EXP'. The expiry date refers to the last day of that month.

Before use:
Store in a refrigerator, between 2 °C and 8 °C.
Do not freeze.

After opening:
Use each pre-filled pen within 28 days of opening. Store below 25 °C.

Always store the pen with the pen cap on, in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What MENOPUR contains

The active substance is highly purified menotrophin (human menopausal gonadotrophin, HMG).

MENOPUR 600 IU solution for injection in pre-filled pen:
One pre-filled multidose pen delivers menotrophin corresponding to follicle stimulating hormone activity FSH 600 IU and luteinizing hormone activity LH 600 IU.

MENOPUR 1200 IU mL solution for injection in pre-filled pen:
One pre-filled multidose pen delivers menotrophin corresponding to follicle stimulating hormone activity FSH 1200 IU and luteinizing hormone activity LH 1200 IU.

The other ingredients are:
- Phenol
- Methionine
- Arginine hydrochloride
- Polysorbate 20
- Sodium hydroxide
- Hydrochloric acid
- Water for injections

What MENOPUR looks like and contents of the pack

MENOPUR is a clear and colourless solution for injection in a pre-filled pen.

MENOPUR 600 IU mL solution for injection in pre-filled pen is available in packs of 1 pre-filled pen and 12 injection needles.

MENOPUR 1200 IU solution for injection in pre-filled pen is available in packs of 1 pre-filled pen and 21 injection needles.

Marketing Authorisation Holder and Manufacturer

<[To be completed nationally]>

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

Manufacturer
Ferring GmbH
Wittland 11, D-24109 Kiel, Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Cyprus, Greece, Denmark, Finland, Iceland, Norway, Portugal, Sweden: Menopur
Italy: Meropur

This leaflet was last revised in <{MM/YYYY}> <{month YYYY}>.

<[To be completed nationally]>

Instructions for Use

MENOPUR® Pre-filled pen

Menotrophin solution for injection

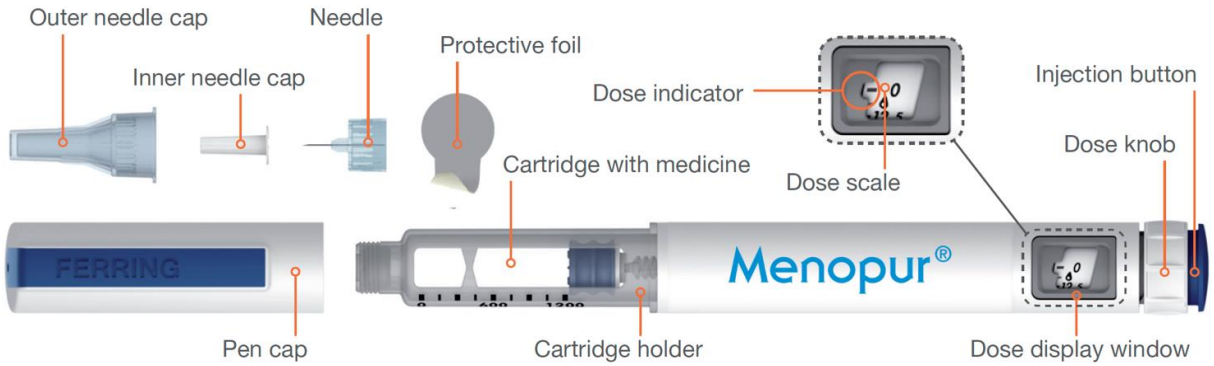
Your healthcare provider (doctor, nurse or pharmacist) should show you how to prepare and inject MENOPUR the right way before you inject it for the first time.

Read this booklet completely before using your MENOPUR pre-filled pen and each time you get a new pen. There may be new information. Follow the instructions carefully even if you have used a similar injection pen before. Using the pen incorrectly could result in receiving an incorrect dose of medicine. Call your healthcare provider if you have any questions about how to give your MENOPUR injection.

The MENOPUR pre-filled pen is a disposable, dial-a-dose pen that can be used to give more than 1 dose of MENOPUR. The numbers you see in the dose display window represent the number of international units (IU) of MENOPUR. The pen is available in 2 different presentations:

• 600 IU
• 1200 IU

MENOPUR pre-filled pen and its parts



Instructions for use – MENOPUR pre-filled pen

Important information

- The MENOPUR pre-filled pen and the needles are for use by only one person and should not be shared with others.
- Use the pen only for the medical condition it is prescribed for and as directed by your healthcare provider.
- If you are blind or have poor eyesight, do not use this pen without help. Get help from a person with good eyesight who is trained to use the pen.

Information about your MENOPUR pre-filled pen

The pen can be dialled to give doses from 6.25 IU to 450 IU of MENOPUR in marked increments of 6.25 IU.

- The dose scale of the pen is numbered from 0 to 450 IU.
- Going from one line that is labelled with a dose to the very next line that does not have a label will increase or decrease the dose by 6.25 IU depending if you are turning the dose up or down. See "Examples of how to dial a dose" on Page 20 to 21[1].
- When turning the dial to your dose, you will hear a click sound and feel resistance on the dial for each increment to help you dial the correct dose.

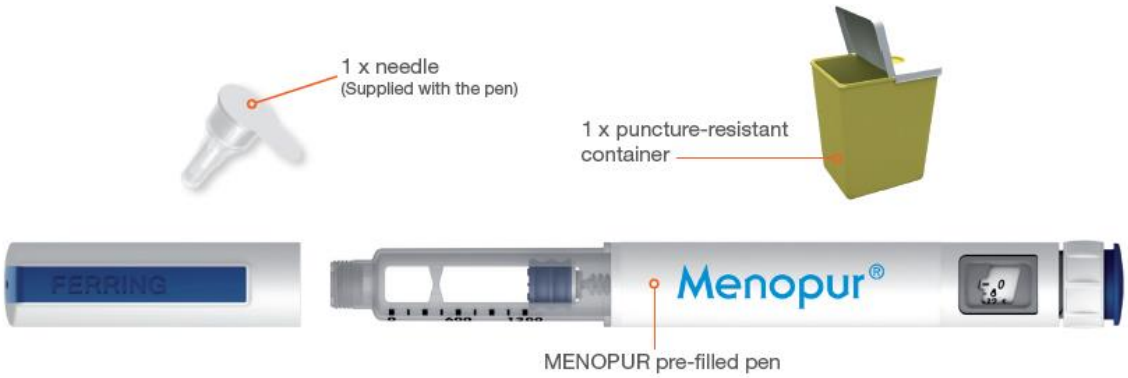
Cleaning

- If needed, the outside of your pen may be cleaned with a cloth moistened with water.
- Do not put the pen in water or any other liquid.

Storage

- Do not freeze.
- Before use, store the pen in a refrigerator between 2 °C to 8 °C.
- After first use, use each pre-filled pen within 28 days and store below 25 °C.
- Always store the pen with the pen cap on and without a needle attached.
- Do not use the pen after the expiration date (EXP) printed on the pen label. The expiration date is the last day of the month of expiration.
- Do not store the pen in extreme temperatures, direct sunlight or very cold conditions, such as in a car or freezer.
- Store the pen out of the sight and reach of children.

Supplies you will need to give your MENOPUR injection

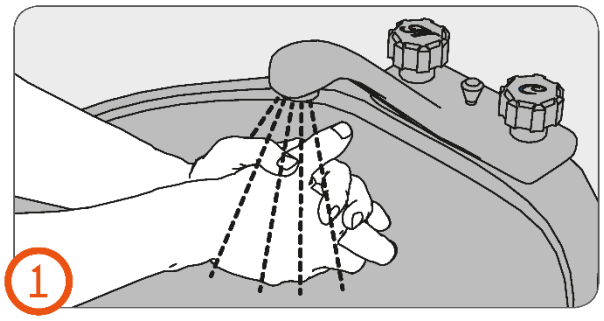


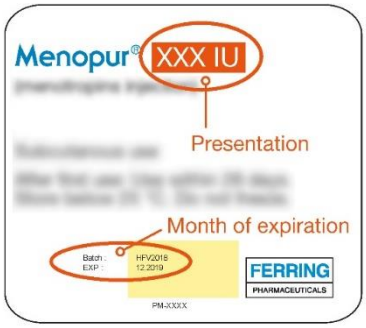
[1] Reference to page numbers is to the printed Instructions For Use booklet

Before use – (Step 1)

1.

- Wash your hands.
- Make sure you have the correct pen with correct presentation.
- Check the expiration on the pen label.





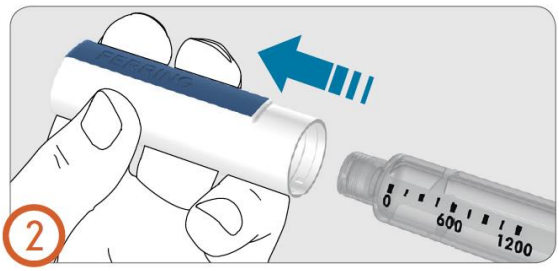
Attaching needle – (Step 2 to 6)

Important:

- Always use a new needle for each injection.
- Only use the single-use click-on needles supplied with the pen.

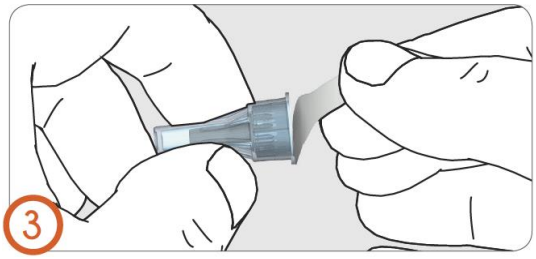
2.

- Pull off the pen cap.
- Check that the pen is not damaged.
- Check that the medicine is clear and does not contain particles.
- Do not use the pen if it is damaged, contains particles or has unclear medicine in the cartridge.



3.

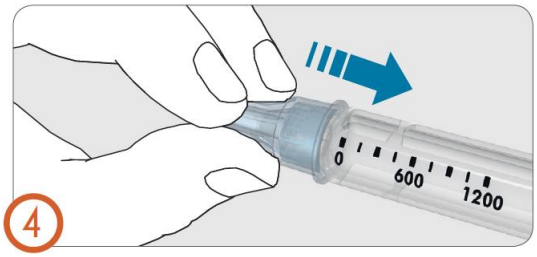
- Pull off the protective foil from the needle.



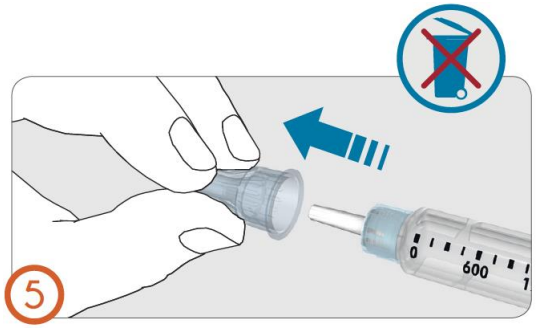
4.

- Click the needle onto the pen.

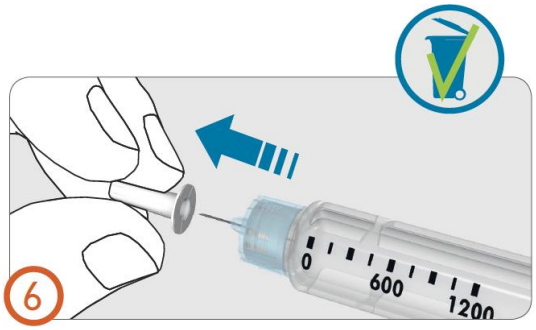
- You will hear or feel a click when the needle is safely on.



5.
- Pull off the outer needle cap.
- Do not throw the outer needle cap away. You will need it to throw away the needle after injecting the medicine.

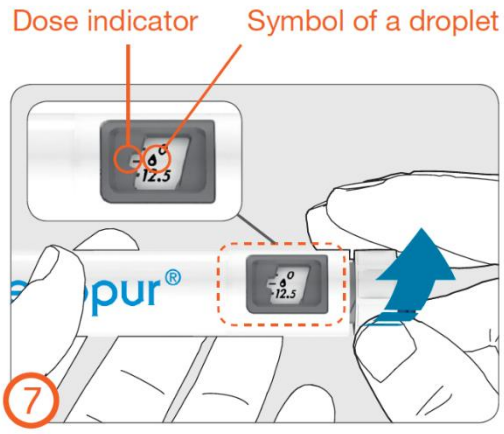


6.
- Pull off the inner needle cap and throw it away.



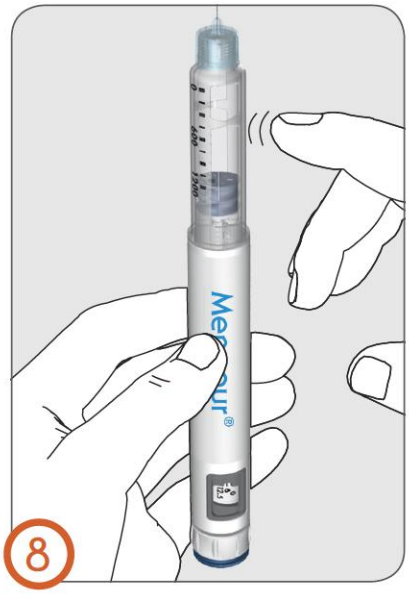
Priming – (Step 7 to 9)
- Before using the pen for the first time, you need to remove air bubbles from the cartridge (Priming) to receive the correct dose of medicine.
- Only prime your pen the first time you use it.
- Perform Step 7 to 9 even if you do not see air bubbles.
- If the pen has already been used go directly to Step 10.

7.
- Turn the dose knob clockwise until a symbol of a droplet lines up with the dose indicator.
- If you dial the incorrect priming dose, the priming dose can be corrected either up or down without loss of medicine by turning the dose knob in either direction until the symbol of a droplet lines up with the dose indicator.



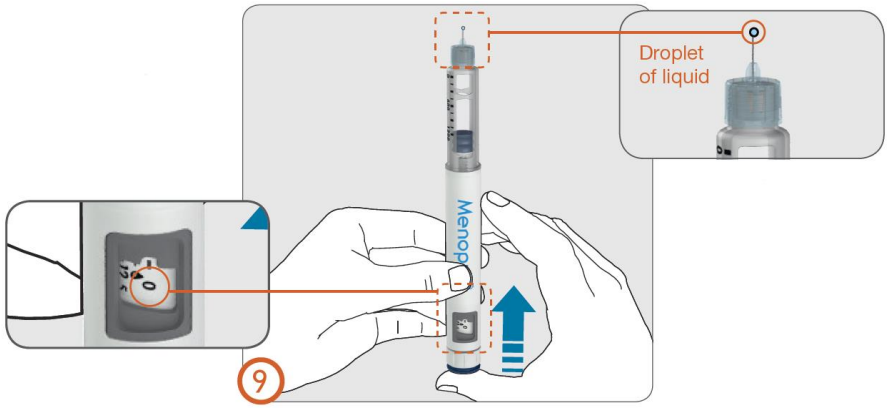
8.

- Hold the pen with the needle pointing upwards.
- Tap with your finger on the cartridge holder to make any air bubbles in the cartridge rise to the top of the cartridge.



9.

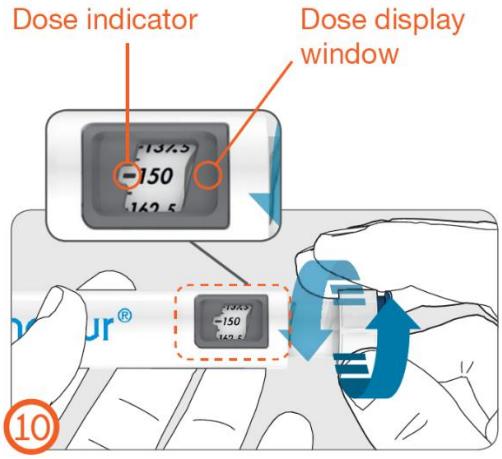
- With the needle still pointing upwards (away from the face) press the injection button all the way in until you see the number ‘0’ lined up with the dose indicator.



- Check that a droplet of liquid appears at the tip of the needle.
- If no droplet(s) appear repeat Steps 7 to 9 (Priming) until a droplet appears.
- If no droplet appears after 5 tries, remove the needle (See Step 13), attach a new needle (See Steps 3 to 6), and repeat priming (See Steps 7 to 9).
- If you still do not see a droplet after using a new needle, try a new pen.

Dialing the dose – (Step 10)

• Turn the dose knob clockwise until the prescribed dose lines up with the dose indicator in the dose display window.
• The dose can be corrected either up or down without loss of medicine by turning the dose knob in either direction until the correct dose lines up with the dose indicator.
• Do not press the injection button when dialling the dose to avoid loss of medicine.
See "Examples of how to dial a dose" on Page 20 to 21[1].



Split-dosing

- You may need more than one pen to complete your prescribed dose.
- If you are not able to dial your complete dose, this means there is not enough medicine left in the pen. You will need to give a split-dose injection or throw away your current pen and use a new pen for your injection.

See "Giving a split-dose of MENOPUR" on Page 22 to 23[1] for examples of how to calculate and record your split dose.

Injecting the dose – (Step 11 to 12)

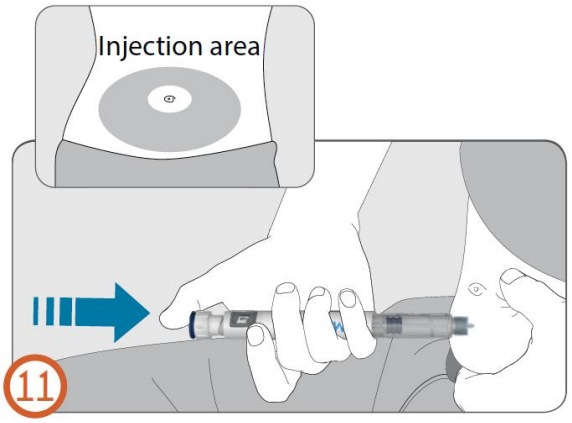
Important:

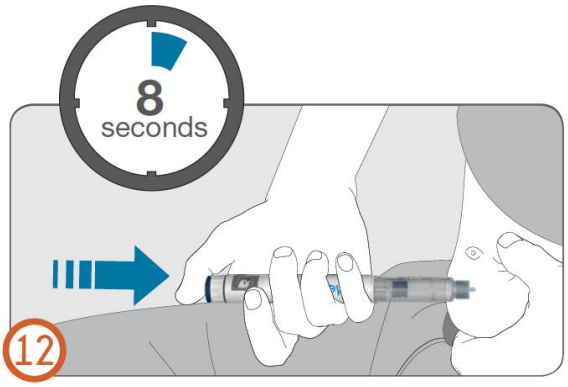
- Read Step 11 and 12 on Page 14 to 15[1] before giving your injection.
- This medicine should be given by injection just under the skin (subcutaneously) in the stomach-area (abdomen).
- Use a new injection site for each injection to lower the risk of skin reactions such as redness and irritation.
- Do not inject into an area that is sore (tender), bruised, red, hard, scarred or where you have stretch marks.

11.

- Hold the pen so the dose display window is visible during injection.
- Pinch your skin and insert the needle straight into your skin as shown by your healthcare provider. Do not touch the injection button yet (See Figure 11).
- After the needle is inserted, place your thumb on the injection button.

- Press the injection button all the way in and hold.
- Keep pressing the injection button in and when you see the number ‘0’ lined up with the dose indicator, wait for 8 seconds (slowly count to 8) (See Figure 12).
  This will make sure you get your full dose.





12.

- After pressing in the injection button for 8 seconds, release the injection button. Then slowly remove the
  needle from the injection site by pulling it straight out of the skin.
- If blood appears at the injection site, press a gauze pad or cotton ball lightly to the injection site.

Note:

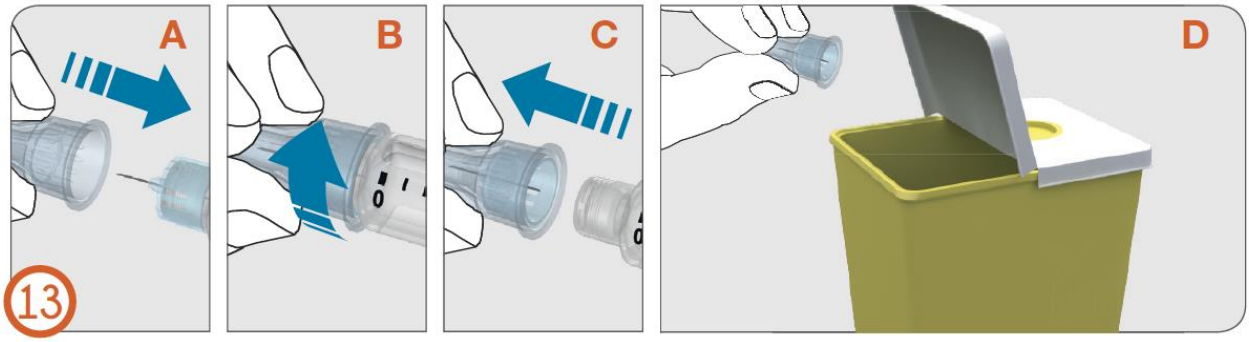
- Do not tilt the pen during injection and removal from skin.
- Tilting the pen can cause the needle to bend or break off.
- If a broken needle remains stuck in the body or remains under the skin, get medical help right away.

Disposal of needle – (Step 13)

13.

- Carefully replace the outer needle cap over the needle with a firm push (see figure 13A).
- Unscrew the needle in counter-clockwise direction to remove the needle from the pen (see figures 13B and 13C).
- Throw away the used needle carefully (see figure 13D).

- See the section, “Disposal” on Page 18[1].

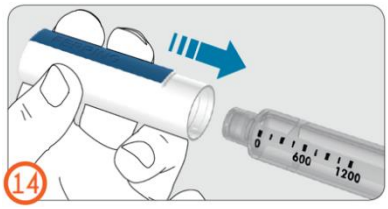


Note:
- Always remove the needle after every use. The needles are for single-use only.
- Do not store the pen with the needle attached.

Replace pen cap – (Step 14)

14.
- Firmly replace the pen cap on the pen for protection between injections

Note:
- The pen cap will not fit over a needle.
- Keep the pen cap on the pen when it is not in use.



Disposal

Needles:
Put your used needles in a puncture resistant container, such as a sharps disposal container right away after use.

If you do not have a sharps disposal container, you may use a household container that is:
- made of a heavy-duty plastic,
- can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labelled to warn of hazardous waste inside the container.

You should dispose of your sharps disposal container when it is almost full. Ask your doctor, nurse or pharmacist for the right way to dispose. Do not throw away your used sharps disposal container in your household trash unless your community guidelines permit this.

MENOPUR pre-filled pens:
- Ask your pharmacist how to throw away medicines you no longer use.

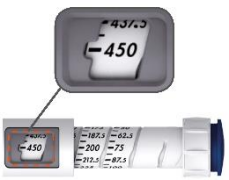
On the following pages, you will find more information on the subjects below[1]:

Examples of how to dial a dose

Examples of how to dial a dose using your MENOPUR pre-filled pen.

The chart to the right shows examples of prescribed doses, how to dial the examples of prescribed doses, and what the dose display window looks like for the prescribed doses.

Examples of prescribed dose (in IU) (units)	Priming dose	75
Dose to dial on pen	Priming symbol (Dial one click starting from 0 until you see the priming symbol of a droplet)	75 (Dial to 75)
Dose display window for example of prescribed dose		

118.75	225	262.5	343.75	450
118.75 (Dial to 112.5 plus 1 click)	225 (Dial to 225)	262.5 (Dial to 262.5)	343.75 (Dial to 337.5 plus 1 click)	450 (Dial to 450)
				

Giving a split-dose of MENOPUR

If you are not able to dial the full prescribed dose in your pen, this means that there is not enough medicine left in the pen to give the full dose. You will need to give part of your prescribed dose using your current pen and the remainder of the dose using a new pen (split-dose injection) or you may throw

away the pen you are using and use a new pen to give your full prescribed dose in 1 injection. If you decide to give a split-dose injection, follow these instructions and write down how much medicine to give using the split-dose diary on Page 23[1].

- Column A shows an example of a prescribed dose. Write down your prescribed dose in column A.
- Column B shows an example of the dose that is left in the pen (this is equal to what you are able to dial).
- Write down the dose that is left in your pen in column B. Give the injection using the rest of the medicine that is left in your pen.
- Prepare and prime a new pen (Step 1 to 9).
- Calculate and write down the remaining dose to inject in column C by subtracting the number in column B from the number in column A. Use a calculator to check your math if needed.
- See "Examples of how to dial a dose" on Page 20 to 21[1] if needed.
- Call your healthcare provider if you have questions about how to calculate your split-dose.
- Inject the remaining dose of medicine (the number in column C) using your new pen to complete your prescribed dose.

Split-dose diary

A Prescribed Dose	**B** Dose left in pen (Dose shown at dose indicator in dose display window)	**C = A minus B** Dose to inject on new pen (Dose shown at dose indicator in dose display window)
112.5	75 (75)	37.5 (37.5)
125	50 (50)	75 (75)
300	181.25 (175 plus 1 line)	118.75 (112.5 plus 1 line)

Frequently Asked Questions (FAQ)

1. Is the priming step necessary before each injection?
   - No. Priming must be performed only before giving the first injection with a new pen.

2. How do I know that the injection is complete?
   - You have pushed the injection button all the way in.
   - The number '0' has lined up with the dose indicator in the dose display window.
   - You have slowly counted to 8 while holding the injection button in and with the needle still in your skin.

3. Why do I have to count to 8 while holding the injection button?
   - Holding the injection button for 8 seconds allows for the full dose to be injected and absorbed under your skin.

4. What if the dose knob cannot be turned to the required dose?
   - The cartridge in the pen may not have enough medicine left to deliver the prescribed dose.
   - The pen does not allow you to dial a larger dose than the dose that is left in the cartridge.
   - You can inject the medicine left in the pen and complete the prescribed dose with a new pen (split-dose) or use a new pen to give the full prescribed dose.

5. What if I do not have enough needles?
- If you need additional needles, contact your healthcare provider. Use only needles that come with your MENOPUR pre-filled pen or that your healthcare provider prescribes.

Warnings

- Do not use a pen if it has been dropped or hit against hard surfaces.
- If the injection button is not easy to push in, do not use force. Change the needle. If the injection button still is not easy to push in after changing the needle, use a new pen.
- Do not try to repair a damaged pen. If a pen is damaged, contact your healthcare provider or local representative of the marketing authorisation holder.

Contact

If you have any questions or problems related to the pen, contact your healthcare provider or local representative of the marketing authorisation holder.

Marketed by:
Local Ferring Company
<[To be completed nationally]>

Revised: <MMM yyyy>

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>