VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

One in six couples experience some form of infertility (problem conceiving) at least once during their lifetime. The major causes of infertility are women who are not ovulating (i.e. not producing eggs), fallopian tube disorders or endometriosis (womb lining cells outside the womb), male factors or unexplained infertility. Not all infertile couples seek treatment. However, advances in assisted reproductive technologies have led to a steady increase in percentage of those undergoing treatment for infertility.

Hormones have been used to stimulate the gonads (gonadotrophins) to treat infertility for about 60 years. Gonadotrophins are used to stimulate the ovaries (or sperm in males) and help ensure that eggs are ready and released at the right time. For women who cannot conceive naturally, eggs which have been made ready can be fertilised outside the woman's body and then placed inside the womb to continue to develop into a baby.

VI.2.2 Summary of treatment benefits

Menotrophin, a natural hormone, is a type of gonadotrophin that helps the reproductive organs to work normally. Ferring menotrophin (MENOPUR or MENOGON) is used to treat the following two groups:

1. Women who do not produce eggs and do not respond to treatment with clomiphene citrate (another medicine that stimulates the ovaries to produce eggs).

2. Women in assisted reproductive technology programmes. Ferring menotrophin helps the ovaries to develop the many egg sacs where an egg might develop.

3. Men who have hypogonadotrophic hypogonadism (a rare hormone deficiency disease) to stimulate sperm production.

Ferring menotrophin has been evaluated in a number of clinical trials and used for more than 20 years in the treatment of infertility where treatment benefits have been well-established. When compared in clinical trials, Ferring menotrophin provided pregnancy rates at least similar to recombinant follicle-stimulating hormone.

VI.2.3 Unknowns relating to treatment benefits

In the main studies nearly all patients were white Caucasians aged between 18 and 40. There is no evidence to suggest that results would be any different in non-white patients.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Overly high levels of activity in the ovaries (Ovarian hyperstimulation syndrome {OHSS})	Ovarian hyperstimulation syndrome occurs when the ovaries over respond to treatment, especially when medicines to trigger ovulation have been used. Symptoms may include feeling sick, weight gain and diarrhoea, or more serious events in severe cases. It occurs in about 12% of female patients, with severe cases occurring in about 4%.	If the ovaries are starting to over respond, medicines to trigger ovulation should not be used.
Severe allergic reactions (Anaphylactic reaction)	Severe allergic reactions are potentially life-threatening if not treated. No cases of severe allergic reactions occurred during clinical trials. Few cases have since been reported, but the chance of this occurring seems to be very low.	Patients may not use Ferring menotrophins if they are allergic to menotrophin or to any of the non-active ingredients. The first injection should be under direct medical supervision.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Using too much medication (overdosage) for MENOPUR 600 IU and 1200 IU products	If the instructions are not properly followed and not all of the solvent is used when preparing MENOPUR 600 IU and 1200 IU products, there is a risk that the concentration of the solution will be too high, resulting in too much medication being used. The chance of this occurring seems to be very low and in the few cases where this has occurred, no undesired effects have been reported.
Blood clots (thromboembolic events {TEE})	These could affect the arteries or veins and can be a complication of ovarian hyperstimulation syndrome. Known risk factors for blood clots include previous having had blood clots, severe obesity, clotting disorders, immobilisation and pregnancy. Untreated blood clots may develop into life-threatening conditions. The chance of this occurring seems to be very low.
Cancer of the reproductive organs	Ovarian cancer is relatively common cancer in women, with about 1 in 70 women eventually developing ovarian cancer and 1 in 100 women die from it. The risk of developing cancer of reproductive system organs is comparatively higher in infertile women seeking infertility treatment. In literature, ovarian and other reproductive organ cancers have been reported in women who have undergone multiple drug treatments for infertility, however, it is not yet known if treatment with gonadotrophins increases the risk of reproductive organ cancers in infertile women.

Missing information

Risk	What is known
Limited information on use in patients with liver or kidney impairment, and metabolic diseases (like diabetes requiring insulin).	Women seeking fertility treatment are generally healthy. Menotrophin, a naturally-occurring hormone, is mainly removed from the body by the kidneys. Ferring menotrophins has been used for more than 20 years with no reports of problems in patients with liver or kidney impairment, and metabolic diseases (like diabetes requiring insulin).

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

For the Summary of Product Characteristics and the Package leaflet for MENOGON or MENOPUR, see Annex 2.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

There are no ongoing or planned post authorisation additional pharmacovigilance studies/activities or efficacy studies/activities in the development plan.

VI.2.7 Summary of changes to the Risk Management Plan over time

There have been no newly identified safety concerns and all safety concerns have previously been included in RMPs. Compared to previous RMP-12 version 3.0 and RMP-16 version 1.0:

- the important potential risks of ‘Thromboembolic event’ and ‘Reproductive system neoplasm’ were added to RMP-12 version 5.0
- the important missing information of ‘Metabolic diseases, such as insulin-dependent diabetes’ was added to RMP-12 version 5.0 and Risk Management Plan version 1.0

- RMP 14 July 2014:
  RMP version 1.0 in ‘EU new RMP template’ dated 5 March 2014 has been updated with editorial changes in Module V and Module VI based on request from RMS/DK in connection with an EU MRP renewal procedure.