

Menopur (menotropins' for injection) – quality defect leading to supply shortage

Dear Healthcare Professional,

FERRING Pharmaceuticals in agreement with the European Medicines Agency and *<insert the name of the regulatory authority(ies), who have approved the communication>* would like to inform you of the following:

Summary

- **In October 2022, Ferring suspended all shipments of Menopur (all presentations). This was a precautionary measure after the company had been made aware of unapproved changes in the manufacturing process of the drug substance of Menopur. This led to a shortage of the medicine which may continue through 2023-2024 in some EU countries.**
- **Ferring is working with National Health Authorities in countries where the product is marketed to obtain the necessary approvals and resume supply.**
- **The data available to date do not indicate any immediate safety issue due to the changes in the manufacturing process.**
- *<In view of the lack of alternatives in several EU Member States and the potential for shortages, batches of Menopur manufactured with unapproved changes will remain on the market in <insert country>.>*
- *<The shortage is expected to continue throughout 2023-2024. While Menopur is unavailable alternatives should be used.>*

Background

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 (CC)
- Controlled ovarian hyperstimulation (COH) 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))
- Stimulation of follicular development in women with hypogonadotropic hypogonadism

Menopur is also indicated for treatment of insufficient spermatogenesis caused by hypogonadotropic hypogonadism in men in some European countries.

Menopur is a highly purified menotropin (menotropin HP) and contains follicle stimulating hormone (FSH) and luteinising hormone (LH) activity in a 1:1 ratio. Menotropin HP induces ovarian follicular growth and development as well as gonadal steroid production in women who do not have primary ovarian failure.

Ferring was made aware of unapproved changes made in the manufacturing process of the drug substance for Menopur. As a precautionary measure, Ferring suspended all shipments of Menopur in October 2022, and the manufacturing at the drug substance supplier was paused for a period of time. The changes include balancing of FSH-LH activity with the addition of highly purified human Chorionic Gonadotropin (hCG). hCG is a naturally occurring hormone which is present in Menopur and contributes to the overall LH activity. The added hCG is the drug substance in Ferring's hCG product (CHORAPUR®/BREVACTID®) licensed in some European countries. Ferring is now working with National Health Authorities in countries where the product is marketed to assess and document the manufacturing changes and update the regulatory file. As a consequence of the pause in manufacturing and validation

steps required for regulatory update, a market shortage of Menopur has occurred. While delivery of Menopur products in some countries has resumed, or is expected to resume in the first half of 2023, shortages are expected to continue throughout 2023 and 2024. Menopur may be out of stock in some countries during this time.

The data available to date do not indicate any immediate safety issue due to the changes in the manufacturing process.

Patients may however still be impacted by shortages of Menopur supply; Ferring continues to work with National Health Authorities to assess and document these changes and resume supply. Individual treatment decisions should be made by healthcare providers. Clinics and patients should check with their preferred pharmacy to confirm they have Menopur availability before initiating treatment. Alternatives to Menopur are available; should a shortage of Menopur occur during treatment, the treating health care professional should evaluate options for further continuation of therapy.

Call for reporting

Section to be completed locally for each national version of the DHPC.

<A reminder of the need and how to report adverse reactions in accordance with the national spontaneous reporting system, including the details (*e.g. name, postal address, fax number, website address*) on how to access the national spontaneous reporting system>

<For biological medicinal products, also include a reminder to report the product name and batch details>

Company contact point

Section to be completed locally for each national version of the DHPC

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Menopur® (highly purified menotropins for injection) MENOPUR 75 IU, 150 IU, 600 IU and 1200 IU powder and solvent for solution for injection MENOPUR 600 IU and 1200 IU solution for injection in pre-filled pen Tradenames: Menopur, Merapur, Meropur, Menogon HP, Menotrophin Ferring, HMG injection, Menotropin
Marketing authorisation holder(s)	Ferring Pharmaceuticals
Safety concern and purpose of the communication	To inform relevant health care professionals of Menopur supply shortage
DHPC recipients	Fertility specialists
Member States where the DHPC will be distributed	EU Member States
Timetable	
DHPC and communication plan (in English) agreed by CMDh	Day 0
Submission of translated DHPCs to the national competent authorities for review	Above + 2 working days
Agreement of translations by national competent authorities	
Dissemination of DHPC	Above + 5 working days