

GONAL- 300 IU/450 IU/900IU

1. NAME OF THE MEDICINAL PRODUCT

- GONAL-f 300 IU/0.5 mL (22 micrograms/0.5 mL) solution for injection in pre-filled pen
- GONAL-f 450 IU/0.75 mL (33 micrograms/0.75 mL) solution for injection in pre-filled pen.
- GONAL-f 900 IU/1.5 mL (66 micrograms/1.5 mL) solution for injection in pre-filled pen.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

GONAL-f 300 IU solution for injection in pre-filled pen: Each ml of the solution contains 600 IU (International Units) of follitropin alfa*. (equivalent to 44 micrograms)

Each pre-filled multidose pen delivers 300 IU (equivalent to 22 micrograms)

GONAL-f 450 IU solution for injection in pre-filled pen:

Each ml of the solution contains 600 IU (International Units) of follitropin alfa, (equivalent to 44 micrograms).

Each pre-filled multidose pen delivers 450 IU (equivalent to 33 micrograms)

GONAL-f 900 IU solution for injection in pre-filled pen:

Each ml of the solution contains 600 IU (International Units) of follitropin alfa, (equivalent to 44 micrograms).

Each pre-filled multidose pen delivers 900 IU (equivalent to 66 micrograms)

* recombinant human follicle stimulating hormone (r-hFSH) produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

3. PHARMACEUTICAL FORM

For the full list of excipients, see section 6.1.

Solution for injection in pre-filled pen. Clear colourless solution. The pH of the solution is 6.7-7.3.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<u>In adult women</u>

- Anovulation (including polycystic ovarian syndrome) in women who have been unresponsive to treatment with clomiphene citrate.
- Stimulation of multifollicular development in women undergoing superovulation for assisted reproductive technologies (ART) such as in vitro fertilisation (IVF), gamete intra-fallopian transfer and zygote intra-fallopian transfer
- GONAL-f in association with a luteinising hormone (LH) preparation is recommended for the stimulation of follicular development in women with severe LH and FSH deficiency. In clinical trials these patients were defined by an endogenous serum LH level < 1.2 IU/L.

• GONAL-f is indicated for the stimulation of spermatogenesis in men who have congenital or acquired hypogonadotrophic hypogonadism with concomitant human Chorionic Gonadotropin (hCG) therapy.

4.2 Posology and method of administration

Treatment with GONAL-f should be initiated under the supervision of a physician experienced in the treatment of fertility disorders

Patients must be provided with the correct number of pens for their treatment course and educated to use the proper injection techniques.

The dose recommendations given for GONAL-f are those in use for urinary FSH. Clinical assessment of GONAL-f indicates that its daily doses, regimens of administration, and treatment monitoring procedures should not be different from those currently used for urinary FSH-containing medicinal products. It is advised to adhere to the recommended starting doses indicated below.

Comparative clinical studies have shown that on average patients require a lower cumulative dose and shorter treatment duration with GONAL-f compared with urinary FSH. Therefore, it is considered appropriate to give: lower total dose of GONAL-f than generally used for urinary FSH, not only in order to optimise follicular development but also to minimise the risk of unwanted ovarian hyperstimulation. See section 5.1.

Bioequivalence has been demonstrated between equivalent doses of the monodose presentation and the multidose presentation of GONAL-f.

Women with anovulation (including polycystic ovarian syndrome)

GONAL-f may be given as a course of daily injections. In menstruating women treatment should commence within the first 7 days of the menstrual cycle.

A commonly used regimen commences at 75-150 IU FSH daily and is increased preferably by 37.5 or 75 IU at 7 or preferably 14 day intervals if necessary, to obtain an adequate, but not excessive, response. Treatment should be tailored to the individual patient's response as assessed by measuring follicle size by ultrasound and/or oestrogen secretion. The maximal daily dose is usually not higher than 225 IU FSH. If a patient fails to respond adequately after 4 weeks of treatment, that cycle should be abandoned and the patient should undergo further evaluation after which she may recommence treatment at a higher starting dose than in the • gynaecological haemorrhages of unknown aetiology abandoned cycle.

When an optimal response is obtained, a single injection of 250 micrograms recombinant human choriogonadotropin alfa (r-hCG) or 5,000 IU, up to 10,000 IU hCG should be administered 24-48 hours after the last GONAL-f 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 is obtained, treatment should be stopped and hCG withheld (see section 4.4). Treatment should recommence in the next cycle at a dose lower than that of the previous cycle.

Women undergoing ovarian stimulation for multiple follicular development prior to in vitro fertilisation or other assisted reproductive technologies.

A commonly used regimen for superovulation involves the administration of 150-225 IU of GONAL-f daily, commencing on days 2 or 3 of the cycle. Treatment is continued until adequate follicular development has been achieved (as assessed by monitoring of serum oestrogen concentrations and/or ultrasound examination), with the dose adjusted according to the patient's response, to usually not higher than 450 IU daily. In general adequate follicular development is achieved on average by the tenth day of

A single injection of 250 micrograms r-hCG or 5,000 IU up to 10,000 IU hCG is administered 24-48 hours after the last GONAL-f injection to induce

Down-regulation with a gonadotropin-releasing hormone (GnRH) agonist or antagonist is now commonly used in order to suppress the endogenous LH surge and to control tonic levels of LH. In a commonly used protocol, GONAL-f is started approximately 2 weeks after the start of agonist treatment, both being continued until adequate follicular development is achieved. For example, following two weeks of treatment with an agonist, 150-225 IU GONAL-f are administered for the first 7 days. The dose is then adjusted according to the ovarian response.

Overall experience with IVF indicates that in general the treatment success rate remains stable during the first four attempts and gradually declines

Women with anovulation resulting from severe LH and FSH deficiency.

In LH and FSH deficient women (hypogonadotrophic hypogonadism), the objective of GONAL-f therapy in association with lutropin alfa is to develop a single mature Graafian follicle from which the oocyte will be liberated after the administration of human chorionic gonadotropin (hCG). GONAL-f should be given as a course of daily injections simultaneously with lutropin alfa. Since these patients are amenorrhoeic and have low endogenous oestrogen secretion, treatment can commence at any time.

A recommended regimen commences at 75 IU of lutropin alfa daily with 75-150 IU FSH. Treatment should be tailored to the individual patient's response as assessed by measuring follicle size by ultrasound and oestrogen

If an FSH dose increase is deemed appropriate, dose adaptation should preferably be after 7-14 day intervals and preferably by 37.5-75 IU increments. It may be acceptable to extend the duration of stimulation in any one cycle to up to 5 weeks.

When an optimal response is obtained, a single injection of 250 micrograms r-hCG or 5,000 IU up to 10,000 IU hCG should be administered 24-48 hours after the last GONAL-fand lutropinal fain jections. The patient is recommended to have coitus on the day of, and on the day following, hCG administration. Alternatively, IUI may be performed.

Luteal phase support may be considered since lack of substances with luteotrophic activity (LH/hCG) after ovulation may lead to premature failure

If an excessive response is obtained, treatment should be stopped and hCG withheld. Treatment should recommence in the next cycle at a dose of FSH lower than that of the previous cycle.

Men with hypogonadotrophic hypogonadism

GONAL-f should be given at a dose of 150 IU three times a week, concomitantly with hCG, for a minimum of 4 months. If after this period, the patient has not responded, the combination treatment may be continued: current clinical experience indicates that treatment for at least 18 months may be necessary to achieve spermatogenesis.

Special population

There is no relevant use of GONAL-f in the elderly population. Safety and effectiveness of GONAL-f in elderly patients have not been established.

Safety, efficacy and pharmacokinetics of GONAL-f in patients with renal or hepatic impairment have not been established.

Paediatric population

There is no relevant use of GONAL-t in the paediatric population.

Method of administration

GONAL-f is intended for subcutaneous use. The first injection of GONAL-f should be performed under direct medical supervision. Self-administration of GONAL-f should only be performed by patients who are well motivated, adequately trained and have access to expert advice.

As GONAL-f pre-filled pen with multidose cartridge is intended for several injections, clear instructions should be provided to the patients to avoid misuse of the multidose presentation.

For instructions on the administration with the pre-filled pen, see section 6.6 and the "Instructions for Use".

4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed
- tumours of the hypothalamus or pituitary gland
- ovarian enlargement or ovarian cyst not due to polycystic ovarian
- ovarian, uterine or mammary carcinoma

GONAL-f must not be used when an effective response cannot be obtained,

- primary ovarian failure
- malformations of sexual organs incompatible with pregnancy
- fibroid tumours of the uterus incompatible with pregnancy
- primary testicular insufficiency

4.4 Special warnings and precautions for use

GONAL-f 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.

Gonadotropin therapy requires a certain time commitment by physicians and supportive health professionals, as well as the availability of appropriate monitoring facilities. In women, safe and effective use of GONAL-f calls for monitoring of ovarian response with ultrasound, alone or preferably in combination with measurement of serum oestradiol levels, on a regular basis. There may be a degree of inter-patient variability in response to FSH administration, with a poor response to FSH in some patients and exaggerated response in others. The lowest effective dose in relation to the treatment objective should be used in both men and women.

Patients with porphyria or a family history of porphyria should be closely monitored during treatment with GONAL-f. Deterioration or a first appearance of this condition may require cessation of treatment.

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 appropriate specific treatment given.

Patients undergoing stimulation of follicular growth, whether as treatment for anovulatory infertility or ART procedures, may experience ovarian enlargement or develop hyperstimulation. to recommended GONAL-f dose and regimen of administration, and careful monitoring of therapy will minimise the incidence of such events. For accurate interpretation of the indices of follicle development and maturation, the physician should be experienced in the interpretation of the relevant tests.

In clinical trials, an increase of the ovarian sensitivity to GONAL-f was shown when administered with lutropin alfa. If an FSH dose increase is deemed appropriate, dose adaptation should preferably be at 7-14 day intervals and preferably with 37.5-75 IU increments

No direct comparison of GONAL-f/LH versus human menopausal gonadotropin (hMG) has been performed. Comparison with historical data suggests that the ovulation rate obtained with GONAL-f/LH is similar to that obtained with hMG

Ovarian Hyperstimulation Syndrome (OHSS)

A certain degree of ovarian enlargement is an expected effect of controlled ovarian stimulation. It is more commonly seen in women with polycystic ovarian syndrome and usually regresses without treatment.

In distinction to uncomplicated ovarian enlargement, OHSS is a condition 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 symptomatology 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, or acute pulmonary distress. Very rarely, severe OHSS may be complicated by ovarian torsion or thromboembolic events such as pulmonary embolism, ischaemic stroke or myocardial infarction.

Independent risk factors for developing OHSS include polycystic ovarian syndrome high absolute or rapidly rising serum oestradiol levels (e.g. > 900 pg/mL or > 3,300 pmol/L in anovulation;

> 3,000 pg/mL or > 11,000 pmol/L in ART) and large number of developing ovarian follicles (e.g. > 3 follicles of ≥ 14 mm in diameter in anovulation: > 20 follicles of > 12 mm in diameter in ART)

Adherence to recommended GONAL-f dose and regimen of administration can minimise the risk of ovarian hyperstimulation (see sections 4.2 and 4.8). Monitoring of stimulation cycles by ultrasound scans as well as oestradiol measurements are recommended to early identify risk factors

There is evidence to suggest that hCG plays a key role in triggering OHSS and that the syndrome may be more severe and more protracted if pregnancy occurs. Therefore, if signs of ovarian hyperstimulation occur such as serum oestradiol level > 5,500 pg/mL or > 20,200 pmol/L and/or ≥ 40 follicles in total, it is recommended that hCG be withheld and the patient be advised to refrain from coitus or to use barrier contraceptive methods for at least Hdays. OHSS may progress rapidly (within 24 hours) or over several days to become a serious medical event. It most often occurs after hormonal treatment has been discontinued and reaches its maximum at about seven to ten days following treatment. Therefore patients should be followed for at least two weeks after hCG administration.

In ART, aspiration of all follicles prior to ovulation may reduce the occurrence of hyperstimulation.

Mild or moderate OHSS usually resolves spontaneously. If severe OHSS occurs, it is recommended that gonadotropin treatment be stopped if still ongoing, and that the patient be hospitalised and appropriate therapy be started.

In patients undergoing ovulation induction, the incidence of multiple pregnancy is increased compared with natural conception. The majority of multiple conceptions are twins. Multiple pregnancy, especially of high order, carries an increased risk of adverse maternal and perinatal outcomes.

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

To minimise the risk of multiple pregnancy, careful monitoring of ovarian

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

Pregnancy loss

The incidence of pregnancy loss by miscarriage or abortion is higher in patients undergoing stimulation of follicular growth for ovulation induction or ART than following natural conception.

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 treatments. The prevalence of ectopic pregnancy after ART, was reported to be higher than in the general population.

Reproductive system neoplasms

There have been reports of ovarian and other reproductive system neoplasms, both benian and malianant, in women who have undergone multiple treatment regimens for infertility treatment. It is not yet Immune system disorders established whether or not treatment with gonadotropins increases the risk Very rare: Mild to severe hypersensitivity reactions including 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

In women with recent or ongoing thromboembolic disease or women with generally recognised risk factors for thromboembolic events, such as personal or family history, treatment with gonadotropins may further increase the risk for aggravation or occurrence of such events. In these women, the benefits of gonadotropin administration need to be weighed against the risks. It should be noted however that pregnancy itself as well as OHSS also carry an increased risk of thromboembolic events.

Elevated endogenous FSH levels are indicative of primary testicular failure. Such patients are unresponsive to GONAL-f/hCG therapy. GONAL-f should not be used when an effective response cannot be obtained.

Semen analysis is recommended 4 to 6 months after the beginning of treatment as part of the assessment of the response. Sodium content

GONAL-f contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially

"sodium-free". 4.5 Interaction with other medicinal products and other forms of

Concomitant use of GONAL-f with other medicinal products used to stimulate ovulation (e.g. hCG, clomiphene citrate) may potentiate the follicular response, whereas concurrent use of a GnRH agonist or antagonist to induce pituitary desensitisation may increase the dose of GONAL-f needed to elicit an adequate ovarian response. No other clinically significant medicinal product interaction has been reported during GONAL-f therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no indication for use of GONAL-f during pregnancy. Data on a limited number of exposed pregnancies (less than 300 pregnancy outcomes) indicate no malformative or feto/neonatal toxicity of follitropin alfa.

No teratogenic effect has been observed in animal studies (see section 5.3). In case of exposure during pregnancy, clinical data are not sufficient to exclude a teratogenic effect of GONAL-f.

Breast-feeding

GONAL-f is not indicated during breast-feeding. Fertility

GONAL-f is indicated for use in infertility (see section 4.1).

4.7 Effects on ability to drive and use machines GONAL-f is expected to have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions are headache, ovarian cysts and local injection site reactions (e.g. pain, erythema, haematoma, swelling and/or irritation at the site of injection).

Mild or moderate ovarian hyperstimulation syndrome (OHSS) has been commonly reported and should be considered as an intrinsic risk of the stimulation procedure. Severe OHSS is uncommon (see section 4.4).

Thromboembolism may occur very rarely (see section 4.4).

List of adverse reactions

The following definitions apply to the frequency terminology used hereafter: very common ($\geq 1/10$), common ($\geq 1/100$ to < 1/10), uncommon $(\geq 1/1,000 \text{ to} < 1/100)$, rare $(\geq 1/10,000 \text{ to} < 1/1,000)$, very rare (< 1/10,000). 5.2 Pharmacokinetic properties

Immune system disorders

Very rare: Mild to severe hypersensitivity reactions including anaphylactic reactions and shock

Nervous system disorders Very common: Headache

<u>Vascular disorders</u> Very rare: Thromboembolism (both in association with and separate from OHSS)

Respiratory, thoracic and mediastinal disorders

Very rare: Exacerbation or aggravation of asthma

section 4.4)

Complication of severe OHSS

anaphylactic reactions and shock

General disorders and administration site conditions

Respiratory, thoracic and mediastinal disorders

Skin and subcutaneous tissue disorders

Reproductive system and breast disorders

Common: Gynaecomastia, Varicocele

Reporting of suspected adverse reactions

Common: Acne

<u>Investigations</u>

Common: Weight gain

Very rare: Exacerbation or aggravation of asthma

General disorders and administration site conditions

a possibility that OHSS may occur (see section 4.4).

5. PHARMACOLOGICAL PROPERTIES

systems, gonadotropins, ATC code: G03GA05.

5.1 Pharmacodynamic properties

the administration of hCG.

compared to urinary FSH.

imber of oocytes retrieved

Need to increase the dose (%)

Days of FSH stimulation required

Clinical efficacy and safety in men

despite unmeasurable LH levels.

tal dose of FSH required (number of F

at least 4 months induces spermatogenesis.

technologies)

75 IU ampoules)

for all criteria listed.

Clinical efficacy and safety in women

LH measurements performed in different laboratories.

period needed to trigger follicular maturation.

Non-clinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity and genotoxicity additional to that already stated in other sections of this SmPC.

> Impaired fertility has been reported in rats exposed to pharmacological doses of follitropin alfa (≥ 40 IU/kg/day) for extended periods, through

reduced fecundity. Given in high doses (≥ 5 IU/kg/day) follitropin alfa caused a decrease in the number of viable foetuses without being a teratogen, and dystocia similar

to that observed with urinary Menopausal Gonadotropin (hMG). However, since GONAL-f is not indicated in pregnancy, these data are of limited clinical relevance.

6. PHARMACEUTICAL PARTICULARS

Sodium dihydrogen phosphate monohydrate

5.3 Preclinical safety data

m-Cresol

Sodium hydroxide Water for injections

6.2 Incompatibilities

6.3 Shelf life

2 years.

6.5 Presentations

Once opened, the medicinal product may be stored for a maximum of 28 days at or below 25°C. The patient should write on the GONAL-f pre-filled pen the day of the first use.

6.4 Special precautions for storage

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

Before opening and within its shelf life, the medicinal product may be removed from the refrigerator, without being refrigerated again, for up to 3 months at or below 25°C. The product must be discarded if it has not been used after 3 months.

For in-use storage conditions, see section 6.3.

Pack of 1 pre-filled pen and 8 needles to be used with the pen for

- GONAL-f 900 IU solution for injection in pre-filled pen:

6.6 Special precautions for disposal and other handling

The solution should not be administered if it contains particles or is not clear. Any unused solution must be discarded not later than 28 days after

GONAL-f 300 IU/0.5 mL (22 micrograms/0.5 mL) is not designed to allow the

efficacy and safety of GONAL-f with urinary FSH in assisted reproduction accordance with local requirements.

Merck Serono S.p.A. Via delle Magnolie 15 (loc. frazione Zona Industriale)

Marketing Authorization Holder in Europe: Merck Europe B.V; Gustav Mahlerplein 102, 1082 MA Amsterdam, Netherlands

27 September 2016

This is a medicine

oduct which affects your health and its consu A medicine is a n contrary to instructions, is dangerous for you. Closely follow your doctor's prescription, the method of use and the

instructions of the pharmacist who sold the product. Your doctor and the pharmacist are experts in medicine, its benefits and risks.

Do not interrupt the period of treatment prescribed without your

doctor's permission.

Do not repeat the same prescription without consulting your doctor.

Union of Arab Pharmacists

Common: Abdominal pain, abdominal distension, abdominal discomfort,

nausea, vomiting, diarrhoea

Reproductive system and breast disorders

Very common: Ovarian cysts Common: Mild or moderate OHSS (including associated symptomatology)

Very common:Injection site reactions (e.g. pain, erythema, haematoma,

Very common:Injection site reactions (e.g. pain, erythema, haematoma

swelling and/or irritation at the site of injection)

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.

The effects of an overdose of GONAL-f are unknown, nevertheless, there is

Pharmacotherapeutic group: Sex hormones and modulators of the genital

In women, the most important effect resulting from parenteral

administration of FSH is the development of mature Graafian follicles. In

women with anovulation, the object of GONAL-f therapy is to develop a

single mature Graafian follicle from which the ovum will be liberated after

In clinical trials, patients with severe FSH and LH deficiency were defined by

an endogenous serum LH level < 1.2 IU/L as measured in a central laboratory.

However, it should be taken into account that there are variations between

In clinical studies comparing r-hFSH (follitropin alfa) and urinary FSH in

ART (see table below) and in ovulation induction, GONAL-f was more potent

GONAL-f

(n = 130)

11.0 ± 5.9

 11.7 ± 1.9

 $5H|27.6 \pm 10.2$

56.2

Differences between the 2 groups were statistically significant (p< 0.05)

In men deficient in FSH, GONAL-f administered concomitantly with hCG for

Following intravenous administration, follitropin alfa is distributed to the

extracellular fluid space with an initial half-life of around 2 hours and

eliminated from the body with a terminal half-life of about one day. The

steady state volume of distribution and total clearance are 10 l and 0.6 l/h,

respectively. One-eighth of the follitropin alfa dose is excreted in the urine.

Following subcutaneous administration, the absolute bioavailability is about

70 %. Following repeated administration, follitropin alfa accumulates 3-fold

achieving a steady-state within 3-4 days. In women whose endogenous

gonadotropin secretion is suppressed, follitropin alfa has nevertheless been

shown to effectively stimulate follicular development and steroidogenesis,

(n = 116)

 8.8 ± 4.8

14.5 ± 3.3

40.7 ± 13.6

85.3

swelling and/or irritation at the site of injection)

Uncommon: Severe OHSS (including associated symptomatology) (see

6.1 List of excipients

Poloxamer 188

Sucrose

Methionine

Disodium phosphate dihydrate

Phosphoric acid, concentrated

Not applicable.

Store in the original package, in order to protect from light.

GONAL-f 300 IU solution for injection in pre-filled pen:

GONAL-f 450 IU solution for injection in pre-filled pen: Pack of 1 pre-filled pen and 12 needles to be used with the pen for

Pack of 1 pre-filled pen and 20 needles to be used with the pen for

Not all presentations may be registered or marketed.

See the "Instructions for Use".

than urinary FSH in terms of a lower total dose and a shorter treatment first opening.

In ART, GONAL-f at a lower total dose and shorter treatment period than cartridge to be removed. urinary FSH, resulted in a higher number of oocytes retrieved when

Discard used needles immediately after injection.

Table: Results of study GF 8407 (randomised parallel group study comparing Any unused medicinal product or waste material should be disposed of in

urinary FSH 7. Manufacturer:

70026 - Modugno (BA) **–** Italy

8. Date of information

Keep medicines out of reach of children. Council of Arab Health Ministers