

Online appendix 1

Advice Quality Assurance*

Checklist / Protocol for dispensing emergency oral contraceptives ("morning-after pill") in self-medication

(English version as of 6 June 2016; translation of the official German version issued 7 October 2015)

- Customer's age: _____ years
- Why is the "morning-after pill" being requested?
 - Sexual intercourse without contraception
 - Condom failure or failure of another barrier method
 - Forgotten "pill" dose →
Brand name of the "pill"®: _____ Number of the forgotten tablet(s) (1–28): _____
Quantity of forgotten tablets: _____ Last dose: ____ hours ago
 - Repeat request (decreased effect, e.g., vomiting within 3 hours of the first dose)
 - Other reason: _____
- Time of the unprotected sexual intercourse (USI):
Date: _____ Time: _____ Hours since USI: _____
<72 hours: 72–120 hours: >120 hours:
- When was the last period? _____ days ago Not known
- Are there any signs of an existing pregnancy?
(If the answer to one of the following questions is "yes" → pregnancy test and/or gynaecologist)
Was the first day of the last period (_____) more than 28 days ago?
 No Yes
Was the last period lighter than normal? No Yes
Was the last period shorter than normal? No Yes
Was the last period otherwise unusual? No Yes
- Are any of the following acute health problems or chronic diseases known?
 - Do you or does anyone in your family have a history of signs of thrombosis?
 No Yes → UPA
 - Persistent vomiting, malabsorption syndromes (e.g., Crohn's disease), severe liver disorder
 No Yes → Doctor



7. Are you currently breastfeeding? No Yes → Break from breastfeeding (UPA: 1 week; LNG: 8 hours)
8. Are you currently (regularly) taking any drugs*? No Yes

If so, which?: _____

*)The efficacy of the emergency oral contraceptive can be decreased if carbamazepine, rifampicin, St. John's Wort/hypericin-containing products, phenytoin, phenobarbital, oxcarbazepine, primidone, ritonavir, efavirenz, nevirapine, or rifabutin are taken at the same time (these are CYP3A4 inducers). In these cases, the option of inserting a copper intrauterine device for emergency contraception should be mentioned. Further details on relevant interactions can be found in the respective Summaries of Product Characteristics (SPCs)³⁻⁵, which are expressly referred to.

9. Have you ever used the "morning-after pill"? No Yes → When was the last time? _____
- If yes:
Were there any side effects/intolerances during its use?
 No
 Yes → gynaecologist or other physician

Pharmacy records

10. "Morning-after pill" dispensed? Yes No Product: _____[®] No
- If not, why (e.g., combination pill forgotten less than 12 hours ago): _____
11. Referred to gynaecologist or on-call medical services? No Yes
- If yes, why _____

12. Comments:

Pharmacy stamp / Date / Name / Signature

Note:

- *)This checklist is meant for advice quality assurance.
- Further information can be found in the respective valid product information sheets (summary of product characteristics and package leaflets)³⁻⁵, which are expressly referred to.
- If there are any further questions, any uncertainties regarding the self-diagnosis or the appropriateness of self-treatment or any questions that go beyond drug dispensing (for example, on copper intrauterine devices, contraception, sexuality or sexually transmitted diseases), the woman should seek advice from a gynaecologist or other physician.
- LNG = levonorgestrel; UPA = ulipristal acetate; USI = unprotected sexual intercourse

Online Appendix 2

A comparison of the emergency contraceptives levonorgestrel (LNG) and ulipristal acetate (UPA)*

Medicinal product (Drug class)	Levonorgestrel (progestogen/progestin)	Ulipristal acetate (progesterone receptor modulator)
Brand products® marketed in Germany (LNG) and EU (UPA)	Levonoraristo® 1.5 mg, PiDaNa® 1.5 mg, Postinor® 1500 µg, unofem HEXAL® 1.5 mg (there are valid German authorisations for others)	ellaOne® 30 mg
Mechanism of action	Suppression of LH increase and therefore ovulation.	Prevention or delay of ovulation, even if the LH increase has already occurred.
Administration	As early as possible and up to 72 hours (3 days) after unprotected sexual intercourse or contraceptive failure.	As early as possible and up to 120 hours (5 days) after unprotected sexual intercourse or contraceptive failure.
Warnings	The next menstrual bleeding can occur a few days earlier (more likely with LNG) or later (more likely with UPA) than expected. If the menstrual bleeding is delayed by more than 7 days, a gynaecologist should be consulted.	
Side effects	Very common (>1/10) with LNG and common (≥1/100 to <1/10) with UPA: delayed menstruation (>7 days), heavier menstruation, spotting and irregular bleeding, dizziness, headaches, feeling of tension in the breasts, nausea, abdominal pain. Common (≥1/100 to <1/10): vomiting.	UPA: also common: affective disorders. For other uncommon (including vision disturbances) and rare side effects of UPA, see SPC and package leaflet*
Interactions	The concomitant administration of CYP3A4 inducers (e.g., rifampicin, phenytoin, phenobarbital, carbamazepine, St John's wort/hypericin, ritonavir, efavirenz) may result in a decreased efficacy and is therefore not recommended.* In these cases, the option of inserting a copper intrauterine device (IUD) for emergency contraception should be mentioned.	
Breastfeeding	LNG passes into breast milk; recommended break from breastfeeding: 8 hours.	UPA passes into breast milk; recommended break from breastfeeding: 1 week
Contraindication	Known hypersensitivity to the active ingredient.	
Additional precautions	The use of LNG and UPA is not recommended in severe liver diseases. In these cases, the option of inserting a copper IUD for emergency contraception should be mentioned.	

	Repeated use of LNG or UPA within the same menstrual cycle is not recommended. It should be avoided due to the undesirably high hormonal load for the patient and potential severe menstrual disorders.	
	Thromboembolic events have been reported following administration of PiDaNa® 1.5 mg [#] . The possibility of such an event occurring should be taken into account in women with other pre-existing risk factors, in particular with evidence of thrombophilia in their medical history or in their family's medical history.	Use in women with severe asthma treated by oral glucocorticoid is not recommended.
Effects on an existing pregnancy	Does not interrupt an existing pregnancy at a dose of 1.5 mg.	Does not interrupt an existing pregnancy at a single dose of 30 mg.

*) Further information can be found in the respective valid product information sheets (Summaries of Product Characteristics (SPCs) and package leaflets³⁻⁵), which are expressly referred to.

[#]) Of note: the current German Postinor® (1.5 mg LNG) and unofem HEXAL® (1.5 mg LNG) SPCs do not contain any information on thromboembolic events.

Notes:

- It has been proven for both substances that efficacy is higher the sooner they are taken after unprotected sexual intercourse or contraceptive failure.
- For levonorgestrel (LNG), there are comprehensive and long-term data experience with regard to efficacy and safety as a non-prescription emergency contraceptive. LNG has been authorised in Germany as an emergency contraceptive since 2000, ulipristal acetate (UPA; in the EU) since 2009.
- The concomitant use of UPA and LNG is not recommended.
- It has not been clearly demonstrated whether UPA within 72 hours following unprotected sexual intercourse (USI) or contraceptive failure is more effective than LNG in terms of pregnancy rates. Relative risk (RR) UPA vs. LNG: 0.63 (95% confidence interval, 0.37–1.07).¹⁰
- Higher body weight or body mass index (BMI):^{7,11}
The European Medicines Agency (EMA) has extensively investigated whether there is a relationship between high body weight or BMI and a loss of efficacy of the “morning-after pill”. Following an analysis of the data available, it came to the conclusion that the “morning-after pill” (based on LNG and UPA) can be used as an emergency contraceptive irrespective of body weight or BMI, and that the current data does not justify any restrictions on use based on a high body weight or BMI.

The corresponding EMA assessment report^{5,11} also states,

- that limited but inconclusive data suggest that there may be reduced efficacy of these medicinal products with increased body weight in women. These data do not however

support a definite conclusion that increased body weight reduces efficacy of emergency contraceptive medicinal products containing LNG or UPA. Therefore, in light of the currently available data, the benefit-risk balance of LNG- or UPA-containing emergency contraceptives remains positive, subject to the warnings and changes to the product information agreed;

- that the available data should be included in the product information sheets but that no restrictions based on body weight or body mass index are currently recommended.

The text for the package leaflets and Summary of Product Characteristics (SmPCs/SPCs) should be amended accordingly:

ellaOne® (UPA)

Package leaflet:

All women should take the emergency contraceptive as soon as possible after unprotected sexual intercourse. There is evidence that ellaOne is less effective in patients with a higher body weight or body mass index (BMI). These data are however limited and not conclusive. Therefore, ellaOne continues to be recommended for all women irrespective of their body weight or BMI.

Summary of Product Characteristics:

Limited and inconclusive data suggest that there may be reduced efficacy of ellaOne with increasing body weight or body mass index (BMI). In all women emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman's body weight or BMI.⁵

The corresponding study results are detailed in section 5.1 of the ellaOne® Summary of Product Characteristics.

Levonorgestrel (LNG)

Package leaflet:

All women should take the emergency contraceptive as soon as possible after unprotected sexual intercourse. There is some data that <trade name> can be less effective in women with a higher body weight or body mass index (BMI). These data are, however, limited and not conclusive. Therefore, <trade name> is recommended for all women, irrespective of their body weight or BMI.

Summary of Product Characteristics:

Limited and inconclusive data suggest that the efficacy of <trade name> can be reduced in women with higher body weight or body mass index (BMI). All women should take the emergency contraceptive as soon as possible following unprotected sexual intercourse, irrespective of the woman's body weight or BMI. (cf. graduated plan decision for levonorgestrel-containing emergency contraceptives dated 5 November 2014.¹²

The corresponding study results are detailed in section 5.1 of the Summary of Product Characteristics (SPCs).

Online Appendix 3

Sources of information on emergency contraception

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Practising gynaecologists

Practising gynaecologists provide information on, among other things, contraceptive methods and the topics of pregnancy, childbirth and family planning.

On-call medical services (www.116117info.de)

The on-call medical service of the Kassenaerztliche Vereinigungen [Associations of Statutory Health Insurance Physicians] can be contacted throughout Germany on the free phone number 116 117 and through the internet (www.116117info.de); regional specifics may have to be taken into account.

Bundeszentrale für gesundheitliche Aufklärung [Federal Centre for Health Education] (www.bzga.de)

The BZgA [Bundeszentrale für gesundheitliche Aufklärung], as the specialised body under the authority of the Federal Ministry of Health and under the supervisory control of the Federal Ministry for Family Affairs, Senior Citizens, Women and Youth, prepares and distributes materials on sex education and family planning. This is its statutory obligation according to the Act on Assistance to Avoid and Cope with Conflicts in Pregnancy. It provides detailed information on contraception, contraceptive failures and on the “morning-after pill” in brochures and online at www.familienplanung.de. In addition, an online information centre finder is provided, which can be used to find the family planning information centre nearest to the searcher’s home:

www.familienplanung.de/verhuetung/verhuetungspannen/

www.familienplanung.de/beratung/beratungsstellensuche/

pro familia (www.profamilia.de)

This association’s sexuality, partnership and family planning network of expertise offers information and materials on contraceptive methods in information centres and online. An information hotline can be contacted round the clock (24/7) on 0 18 05 / 77 63 26 (+49 (0) 221 8992-0) and offers advice in other languages than German as well (e.g., Turkish, Russian and English).

donum vitae (www.donumvitae.org)

This institution offers advice and help on pregnancy. A flyer on the “morning-after pill” is available for download from the internet:

[http://www.nrw-donumvitae.de/fileadmin/Konzepte/PI\)Ile_Danach_nrw_Flyer_Apotheke.pdf](http://www.nrw-donumvitae.de/fileadmin/Konzepte/PI)Ile_Danach_nrw_Flyer_Apotheke.pdf).

Berufsverband der Frauenärzte e. V. (BVF [Association of German Gynaecologists])
(www.frauenaerzte-im-netz.de)

The BVF provides, in cooperation with the German Society for Gynaecology and Obstetrics (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe, DGGG), help via its website for finding gynaecologists or medical facilities throughout Germany as well as information on methods of contraception and on the subjects of pregnancy, childbirth and family planning.

Summaries of Product Characteristics (SPCs) and package leaflets³⁻⁵

PharmNet.Bund (www.pharmnet-bund.de)

Summaries of product characteristics (SPCs) and package leaflets for medicinal products as well as public assessment reports or reports of clinical studies are also made available to the public via the Portal für Arzneimittelinformationen des Bundes und der Laender [Drug Information Portal of the Bund (Federal Government) and the Laender (States)].

The product information sheets are also made available on the internet at www.fachinfo.de (DocCheck password required, health professionals only), on the websites of the pharmaceutical companies (DocCheck password) and, for medicinal products that are centrally authorised in the EU (such as ellaOne[®]), on the website of the European regulatory authority, the European Medicines Agency (EMA), at www.ema.europa.eu → Find medicine → Human medicines → European public assessment reports (EPAR).