

## ATTACHMENT B

### MTF Formulary Management for Oral Contraceptives and Miscellaneous Contraceptives

Defense Health Agency Pharmacy Operations Division

#### Bottom Line

- New generic and branded entrants to the market since 2013 (e.g., chewable tablets, intermediate strength estrogen formulations (EE 25 mcg), and products with folate and iron supplementation) do not offer clinically significant advantages over oral contraceptive products (OCPs) currently available on the Uniform Formulary (UF).
- The chewable OCPs Minastrin 24 Fe and Generess Fe were designated nonformulary (NF) since they do not offer clinically significant advantages over the non-chewable formulations on the UF.
- AB-rated generics to Jolessa (Quasense, Introvale, and Setlakin) are now UF (previously designated NF).
- No other changes to the contraceptives drug class were made from previous Basic Core Formulary (BCF), UF, or NF designations established at the August 2011 P&T Committee meeting.
- Significant generic competition exists and only 8 branded proprietary products remain in the class.

**Uniform Formulary Decision:** The Director, DHA, approved the recommendations from the February 2016 DoD P&T Committee meeting on May 5, 2016, with an implementation date of August 10, 2016.

Uniform Formulary (UF) Agents		Nonformulary (NF) Agents
Basic Core Formulary (BCF) MTFs <u>must</u> have on formulary	Not on BCF MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
<b>Monophasics with EE 20 mcg</b>		
<ul style="list-style-type: none"> <li>▪ LNG 0.1mg (Sronyx, Lutera, generics)</li> <li>▪ DRSP 3mg (Yaz, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ NETA 1mg (Microgestin Fe 1/20, generics; Microgestin 1/20, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ NETA 1mg (<b>Minastrin 24 Fe chewable</b>)*</li> <li>▪ NETA 1 mg (Lomedia 24 Fe, generics)</li> <li>▪ DRSP 3mg and levomefolate 0.451mg (<b>Beyaz</b>)*</li> </ul>
<b>Monophasics with EE 25 mcg</b>		
		<ul style="list-style-type: none"> <li>▪ NETA 0.8mg (Generess Fe chewable, generics)</li> </ul>
<b>Monophasics with EE 30 mcg</b>		
<ul style="list-style-type: none"> <li>▪ <b>Mono + EE 30mcg CPs</b> <ul style="list-style-type: none"> <li>○ LNG 0.15mg (Levora-28, generics)</li> <li>○ DRSP 3mg (Yasmin 28, generics)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▪ NGT 0.3mg (Low-Ogestrel, generics)</li> <li>▪ NETA 1.5mg (Microgestin Fe 1.5/30, generics; Microgestin 1.5/30, generics)</li> <li>▪ DSG 0.15mg (Reclipsen, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ DRSP 3mg and levomefolate 0.451 mg (<b>Safyral</b>)*</li> </ul>
<b>Monophasics with EE 35 mcg</b>		
<ul style="list-style-type: none"> <li>▪ NGM 0.25mg (Mononessa, generics)</li> <li>▪ NETA 1mg (Norinyl 1+35, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ ETYD 1mg (Zovia 1-35E, generics)</li> <li>▪ NET 0.5mg (Nortrel 0.5/35, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ NET 0.4mg (Balziva, generics)</li> <li>▪ NETA 0.4mg (Wymzya Fe chewable, generics)</li> </ul>
<b>Monophasics with EE 50 mcg</b>		
	<ul style="list-style-type: none"> <li>▪ ETYD 1mg/EE 50mcg (Zovia 1-50E, generics)</li> <li>▪ NGT 0.5mg/EE 50mcg (Ogestrel, generics)</li> <li>▪ NET 1mg/mestranol 50mcg (Norinyl 1+50, generics)</li> </ul>	
<b>Extended Cycle/Continuous Use</b>		
<ul style="list-style-type: none"> <li>▪ LNG 0.15mg/ EE 30mcg (Jolessa ONLY)</li> </ul>	<ul style="list-style-type: none"> <li>▪ LNG 0.15mg/ EE 30mcg (Introvale, Quasense, Setlakin, generics)</li> </ul>	<ul style="list-style-type: none"> <li>▪ LNG 0.09mg/EE 20mcg (Amethyst, generics)</li> <li>▪ LNG 0.15mg/EE 30/10mcg (Camrese, generics)</li> <li>▪ LNG 0.1mg/EE 20/10mcg (Camrese Lo, generics)</li> </ul>
<b>Multiphasics</b>		
<p><u>TRIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ NGM 0.18/0.215/0.25mg/EE 35mcg (TriNessa, generics)</li> </ul>	<p><u>BIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ NET 0.5/1mg/EE 35 mcg (Necon 10/11, generics)</li> <li>▪ DSG 0.15mg/EE 20/10mcg (Azurette, generics)</li> </ul> <p><u>TRIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ DSG 0.1/0.125/0.15mg/EE 25mcg (Velivet, generics)</li> <li>▪ NGM 0.18/0.215/0.25mg/EE 25mcg (Ortho Tri-Cyclen Lo, generics)</li> <li>▪ NET 0.5/0.75/1mg/EE 35mcg (Necon, generics)</li> <li>▪ NET 0.5/1/0.5mg/EE 35mcg (Leena, generics)</li> <li>▪ LNG 0.05/0.075/0.125mg/EE 30/40/30mcg (Trivora-28, generics)</li> </ul> <p><u>QUADRIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ LNG 0.15mg/EE 20/25/30/10mcg (<b>Quartette</b>)</li> </ul>	<p><u>BIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ NETA 1mg/EE 10mcg (<b>Lo Loestrin Fe</b>)*</li> </ul> <p><u>TRIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ NETA 1mg/EE 20/30/25mcg (Tri-Legest Fe, generics)</li> </ul> <p><u>QUADRIPHASIC</u></p> <ul style="list-style-type: none"> <li>▪ DNG 2/3mg/EV 3/2/2/1mg (<b>Natazia</b>)*</li> </ul>

Uniform Formulary (UF) Agents		Nonformulary (NF) Agents
Basic Fore Formulary (BCF) MTFs <u>must</u> have on formulary	Not on BCF MTFs <u>may</u> have on formulary	MTFs <u>must not</u> have on formulary
<b>Progestogen-Only</b>		
▪ NET 0.35mg (Nor-QD, Jolivette, generics)		
<b>Miscellaneous (vaginal ring, transdermal patch, injection)</b>		
	<ul style="list-style-type: none"> <li>▪ ETN 0.12mg/EE 15mcg per day (<b>NuvaRing</b>)*</li> <li>▪ NRL 150mcg/EE 35mcg per day (<b>Xulane</b>)* – equivalent to discontinued Ortho Evra patch</li> <li>▪ DMPA 150mg/mL intramuscular injection (Depo-Provera, generics)</li> <li>▪ DMPA 104mg/0.65mL subcutaneous injection (<b>Depo-SubQ Provera 104</b>)*</li> </ul>	
*Drugs that are in <b>bold font</b> currently do not have AB-rated generics available on the market.		
<b>Abbreviations:</b>		
OCPs-oral contraceptive products	EE-ethinyl estradiol	NET-norethindrone
DNG-dienogest	ETN-etonogestrel	NETA-norethindrone acetate
DMPA-depot medroxyprogesterone acetate	ETYD-ethynodiol diacetate	NGM-norgestimate
DRSP-drospirenone	EV-estradiol valerate	NGT-norgestrel
DSG-desogestrel	LNG-levonorgestrel	NRL-norelgestromin

## Clinical Summary

- There were no significant updates to the previous clinical conclusions from the August 2011 Uniform Formulary class review. See previous P&T Committee meeting minutes for full clinical conclusions.
- Monophasic, extended cycle/continuous use, multiphasic, and progestogen-only oral contraceptives (OCPs) do not appear to have any clinically significant differences in efficacy.
  - Phasic formulations aim to mimic a normal menstrual cycle
  - Extended cycle/continuous use regimens may provide better relief of menstrual symptoms (e.g., headache, bloating, pain, tiredness), but less control of initial breakthrough bleeding
  - Combination products containing < 20 mcg of ethinyl estradiol may offer less effective cycle control compared to higher estrogen-containing OCPs
  - Multiphasic OCPs are associated with better control of breakthrough bleeding
  - Progestogen-only OCPs are a better option for women > 35 years of age or those who need to avoid estrogen, but are associated with more breakthrough bleeding
- Miscellaneous products (transdermal patch, vaginal ring, and both IM and SC depot medroxyprogesterone acetate (DMPA) injections) offer the benefit of an alternate route of administration for certain patient populations, sustained drug delivery, and dosing convenience to reduce or stop menstrual bleeding.
  - Both NuvaRing and the Xulane transdermal patch offer similar contraceptive effectiveness compared to OCPs; they are applied weekly for three weeks, with one week off every 28 days.
  - The DMPA injections are available for either intramuscular or subcutaneous administration. Both formulations are equally efficacious; the DMPA injections provide improved contraceptive effectiveness compared to OCPs and are administered every 90 days.
- While the contraceptives have not been well studied in obese patients, the DMPA injections are associated with fewer overall pregnancy failure rates compared to the oral, ring, and patch methods of contraception.
- All chewable OCPs, Minastrin 24 Fe, Generess Fe, Wymzya Fe, and their respective generics are designated as nonformulary. They will be approved with prior authorization (PA) and medical necessity (MN) criteria for patients with established swallowing difficulties or who are otherwise unable to meet their needs with a formulary alternative monophasic or multiphasic formulation. Refer to P&T Committee meeting minutes or respective PA/MN documents (upon implementation) for details.

## Safety

- Overall, all contraceptive formulations have similar safety and adverse profiles, such as breakthrough bleeding, bloating, nausea, breast tenderness (which may subside after several months), headache, migraine, weight changes, and abnormal carbohydrate/lipid metabolism.

- A two-fold increase in risk of venous thromboembolism may be associated with OCPs containing certain progestins (e.g., desogestrel, drospirenone), as well as with the transdermal patch.
- The Xulane transdermal patch, which is equivalent to the discontinued Ortho Evra patch, is associated with application site reactions and breast tenderness. The NuvaRing vaginal ring is associated with vaginal infections/secretions/irritation, but has fewer metabolic changes than the OCPs.
- Compared to the OCPs, DMPA injections are associated with more bloating, progressively significant weight gain, and are not immediately reversible (fertility may be delayed up to 10-18 months following the last injection).
- Boxed warnings for the OCPs, vaginal ring, and patch include the increased risk of serious cardiovascular events in women who smoke, especially those aged > 35 years who are heavy smokers (>15 cigarettes per day). The DMPA injections have boxed warnings for the following:
  - (1) loss of bone mineral density, which may not be 100% reversible,
  - (2) unknown if use in adolescence/early adulthood will reduce peak bone mass or increase risk of bone fracture in later life, and
  - (3) use longer than 2 years is not recommended unless use of other contraceptive methods are inadequate
- Absolute contraindications to the contraceptives include smoking in ages > 35 years, history of breast cancer/stroke/ischemic heart disease/severe hypertension, active liver disease, undiagnosed abnormal uterine bleeding, known or suspected pregnancy/estrogen-dependent tumor, headaches with focal neurologic symptoms, thromboembolic disorders, and major surgery with prolonged immobilization.

## Overall Conclusion

- Oral and miscellaneous contraceptives are highly effective in preventing pregnancy when used as directed and have comparable efficacy and benefits, while also offering non-contraceptive benefits. Hence, contraceptive choice depends on an individual patient's needs and characteristics, dosing convenience, and/or the need for non-contraceptive benefits.

## References

- DoD P&T Committee minutes: <http://www.health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee: <http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee>
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: [dha.jbsa.pharmacy.list.poduf@mail.mil](mailto:dha.jbsa.pharmacy.list.poduf@mail.mil)

Contraceptives Price Comparison at MTF	
Drug	MTF Cost/Month (Feb 2016)
<b>Uniform Formulary</b>	
<ul style="list-style-type: none"> <li>▪ Oral contraceptives on the BCF</li> <li>▪ DMPA injections on the UF</li> </ul>	<b>\$ Most Cost-Effective</b>
<ul style="list-style-type: none"> <li>▪ All other UF contraceptives</li> </ul>	<b>\$\$ - \$\$\$ Less Cost-Effective</b>
<ul style="list-style-type: none"> <li>▪ Vaginal ring (etonogestrel 0.12mg/EE 15mcg/24 hr (NuvaRing))</li> <li>▪ Transdermal patch (norelgestromin 150mcg/EE 35mcg/24 hr (Xulane))</li> </ul>	<b>\$\$\$\$ Least Cost-Effective</b>
<i>(MTFs should purchase the most cost-effective, contracted, AB-rated bioequivalent products.)</i>	
<b>Nonformulary</b>	
<ul style="list-style-type: none"> <li>▪ <b>Monophasics with EE 20 mcg</b> <ul style="list-style-type: none"> <li>○ norethindrone acetate 1mg (Minastrin 24 Fe; Lomedia 24 Fe, generics)</li> <li>○ drospirenone 3mg and levomefolate 0.451mg (Beyaz)</li> </ul> </li> </ul>	<b>\$\$\$\$ Least Cost-Effective</b>
<ul style="list-style-type: none"> <li>▪ <b>Monophasics with EE 25 mcg</b> <ul style="list-style-type: none"> <li>○ norethindrone acetate 0.8mg (Generess Fe, generics)</li> </ul> </li> </ul>	
<ul style="list-style-type: none"> <li>▪ <b>Monophasics with EE 30 mcg</b> <ul style="list-style-type: none"> <li>○ drospirenone 3mg and levomefolate 0.451mg (Safyral)</li> </ul> </li> </ul>	
<ul style="list-style-type: none"> <li>▪ <b>Monophasics with EE 35 mcg</b> <ul style="list-style-type: none"> <li>○ norethindrone acetate 0.4mg (Balziva, generics)</li> <li>○ norethindrone 0.4mg (Wymzya Fe, generics)</li> </ul> </li> </ul>	
<ul style="list-style-type: none"> <li>▪ <b>Extended Cycle/ Continuous Use</b> <ul style="list-style-type: none"> <li>○ levonorgestrel 0.09mg/EE 20mcg (Amethyst, generics)</li> <li>○ levonorgestrel 0.15mg/EE 30/10mcg (Camrese, generics)</li> <li>○ levonorgestrel 0.1mg/EE 20/10mcg (Camrese Lo, generics)</li> </ul> </li> </ul>	
<ul style="list-style-type: none"> <li>▪ <b>Multiphasics</b> <ul style="list-style-type: none"> <li>○ norethindrone acetate 1mg/EE 10mcg (Lo Loestrin Fe)</li> <li>○ norethindrone acetate 1mg/EE 20/30/25mcg (Tri-Legest Fe, generics)</li> <li>○ dienogest 2/3mg/EV 3/2/2/1mg (Natazia)</li> </ul> </li> </ul>	