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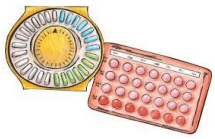

Contraceptive advice for women on potentially teratogenic drugs. The UK Faculty of Sexual & Reproductive Healthcare's Clinical Effectiveness Unit (FSRH CEU) has produced recommendations which can be used to support clinicians who provide contraceptive advice to women using drugs with known or potential teratogenic effects **www.fsrh.org/standards-and-guidance/clinical-statements/contraception-for-specific-populations/**. The recommendations for women using (or whose partners are using) known or potentially teratogenic drugs are as follows:

- Women should be advised that **no method of contraception is 100% effective**
- Contraceptive methods that are considered "highly effective" include the long-acting reversible contraceptives (**LARC**) [copper intrauterine device (**Cu-IUD**), levonorgestrel intrauterine system (**LNG-IUS**) and the progestogen-only implant (**IMP**)] and male and female sterilisation. **These all have a failure rate of <1% with typical use**; however women using IMP must not take any interacting drugs that could reduce contraceptive effectiveness
- Additional contraceptive precautions (e.g. **condoms**) are not required if the above methods of contraception are being used; however a couple may choose to use condoms in addition to further reduce the risk of an unintended pregnancy and **for protection against sexually transmitted infections**
- **The typical use failure rate is 9% for combined hormonal contraception (CHC), 9% for the progestogen-only pill (POP) and 6% for progestogen-only injectables including depot medroxyprogesterone acetate.** Women using these contraceptives should be advised to use additional contraceptive precautions (e.g. condoms) and **should also be advised not to take any interacting drugs that could reduce contraceptive effectiveness**
- The use of barrier methods, withdrawal and fertility awareness methods alone is not recommended.

[**Editor's note**: readers are reminded that the FSRH has many useful guidance documents on contraception available at: **www.fsrh.org/home/**]

Omega-3 fatty acids have little or no effect on cardiovascular disease*.** Although previous studies have suggested benefits on cardiovascular (CV) health with use of omega-3 polyunsaturated fatty acids from oily fish (long-chain omega-3 (LC/omega3), including eicosapentaenoic acid (**EPA**) and docosahexaenoic acid (**DHA**)) and plants (alpha-linolenic acid (**ALA**)), more recent studies have not confirmed this. A recent Cochrane review assessed the effects of increased intake of fish- and plant-based omega-3 for all-cause mortality, CV events, adiposity and lipids (Cochrane Database of Systematic Reviews 2018; Issue 7. Art. No. CD003177***). A total of 79 randomised controlled trials (n=112,000 subjects) were included in the review; trials were of 12 to 72 months' duration and included adults of varying CV risk, mainly in high-income countries. Most studies assessed LC/omega3 supplementation by capsule, but some used LC/omega3 - or ALA-rich foods or dietary advice compared to placebo or usual diet. Primary outcomes included all-cause, CV or coronary heart disease (CHD) mortality; CV events; CHD events; stroke and arrhythmia (atrial fibrillation). **Results** showed little or no effect of increasing LC/omega3 on any of the primary outcomes; increasing ALA levels appeared to be associated with slightly reduced CV events (from 4.8% to 4.7%) with reduced CHD mortality (from 1.1% to 1.0%), and arrhythmia (from 3.3% to 2.6%). LC/omega3 appeared to slightly reduce triglycerides and to increase HDL. The authors conclude that **these findings suggest that increasing EPA and DHA has little or no effect or CV mortality or morbidity (based on moderate-and high-quality evidence), while low-quality evidence suggests ALA may slightly reduce CV event risk, CHD mortality and arrhythmia.** Previous study findings suggesting benefit appear to spring from trials with higher risk of bias.

Cardiovascular safety of febuxostat vs. allopurinol. Patients with gout have an increased risk of cardiovascular (CV) events including death, compared to patients without gout. Allopurinol and febuxostat are used for the management of hyperuricaemia in patients with gout. Early clinical trials suggested a modestly higher rate of CV events with febuxostat compared with either allopurinol or placebo. Recently, a US multicentre randomised controlled trial evaluated whether febuxostat was non-inferior to allopurinol in relation to CV events, in patients with gout and CV disease ***(NEJM 2018; 378: 1200-10).*** Patients (n=6,198) with gout and a history of major CV disease (e.g. previous myocardial infarction or stroke) were randomly assigned to receive febuxostat or allopurinol; patients were stratified according to kidney function and doses of allopurinol were modified according to kidney function. The primary endpoint was a composite of first occurrence of CV death, nonfatal myocardial infarction, nonfatal stroke or urgent revascularisation for unstable angina; secondary safety endpoints included a composite of CV death, nonfatal MI or nonfatal stroke and the individual components of the primary endpoint. The study found that, after a median of 32 months' follow-up, **the primary endpoint occurred in 10.8% of the febuxostat group and 10.4% of the allopurinol group**: therefore febuxostat was found to be non-inferior to allopurinol for the primary endpoint. However, **the risk of death from any cause and the risk of CV death were higher in the febuxostat than the allopurinol group**; hazard ratio (HR) for death from any cause was 1.22 (95% CI, 1.01 to 1.47) and the HR for CV death was 1.34 [95% CI, 1.03 to 1.73) for the febuxostat group. The authors of the study report that the mechanism underlying the risk of death is unclear. Important **limitations of the trial** included the fact that a large number of patients discontinued trial treatment prematurely (56.5%) and a large number did not complete follow-up (45%), however these findings were similar in both groups.

[**Editor's note**: Prescribers are reminded that **treatment with febuxostat in patients with ischaemic heart disease or congestive heart failure is not recommended** – see the Summary of Product Characteristics of febuxostat for full information (**www.medicines.ie** and **www.hpra.ie**). In general, guidelines [including The British Society for Rheumatology Guideline on the management of gout which was updated in 2017 ***(Rheumatology 2017; 56: e1-e20)***] recommend that **allopurinol should be considered as first-line for urate lowering therapy in patients with gout**.]

Information on cannabis for medical use now available. The Dept. of Health has recently published an information document for patients and healthcare professionals on cannabis for medical use (***https://health.gov.ie/blog/publications/cannabis-for-medical-use/***). The document outlines the difference between the main active components of cannabis: **THC** (tetrahydrocannabinol, the main psychoactive constituent of cannabis, which is subject to the Misuse of Drugs legislation) and **CBD** (cannabidiol, which is not psychoactive and therefore does not require a ministerial licence for use). The document also provides guidance on the **application process for a ministerial licence for medical cannabis**. A *Medical Cannabis Access Programme* is currently under development which will facilitate access to cannabis products for specified medical conditions under expert medical supervision (spasticity associated with multiple sclerosis, resistant to all standard therapies; chemotherapy-related intractable nausea and vomiting; severe, refractory epilepsy). A document entitled "***Clinical Guidance on Cannabis for Medical Use***" has also been developed to facilitate the medical use access programme once it has been established. Download it at: **https://health.gov.ie/wp-content/uploads/2018/07/Clinical-guidance-on-cannabis-for-medical-use.pdf**

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This ***newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH.*** *Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie*