## Precautions and Risk Mitigation with Estrogen Therapy:

Several pre-existing medical conditions and risk factors may increase the risks associated with estrogen administration. When these are present, a careful evaluation of risks and benefits should be completed and fully discussed with the client. All reasonable measures should be taken in order to reduce the risks associated with the particular condition. Table 4 summarizes the precautions (i.e. relative contraindications) with estrogen therapy as well as suggested measures that may be taken by the primary care provider to minimize these risks including the involvement of specialists if available. A number of these precautions are expanded upon below.

**Table 4.**
**Precautions with estrogen therapy and suggested measures to minimize associated risks**

| Precaution to Estrogen Therapy | Suggested Measures to Minimize Associated Risks |
|---|---|
| Stable ischemic cardiovascular disease* | Consider referral to cardiology, ensure optimal medical (including prophylactic anticoagulation) and/or surgical management as indicated, aggressive risk factor optimization, use transdermal route of administration +/- lower dose |
| Cerebrovascular disease* | Consider referral to neurology, ensure optimal medical management (including prophylactic anticoagulation) and aggressive risk factor optimization, use transdermal route of administration +/- lower dose |
| Personal history of DVT or PE, hypercoagulable state | Identify and minimize co-existent risk factors, consider prophylactic anti-coagulation, consider referral to hematology, use transdermal route of administration +/- lower dose |
| Marked hypertriglyceridemia | Identify and address barriers to optimal lipid control, refer to dietician, minimize alcohol consumption, consider anti-lipemic pharmacologic therapy, consider endocrinology referral, encourage deferral of estrogen until controlled, consider transdermal route of administration |
| Uncontrolled high blood pressure | Identify and address barriers to optimal BP control, use spironolactone as anti-androgen, add additional antihypertensives as needed (avoid ACEs/ARBs with spironolactone), encourage deferral of estrogen until controlled, consider cardiac stress test, consider transdermal route of administration |
| Uncontrolled diabetes | Identify and address barriers to optimal glycemic control, refer to dietician, encourage lifestyle modification, initiate antiglycemic agent(s), encourage deferral of estrogen until controlled, consider cardiac stress test, consider transdermal route of administration |
| Smoker | Encourage and support smoking cessation, offer NRT and/or bupropion/varenacline, or negotiate a decrease in smoking, consider lower dose, consider cardiac stress test, use transdermal route of administration |
| Family history of abnormal clotting | Consider referral to hematology, rule out genetic clotting disorder, consider prophylactic anticoagulation, use transdermal route of administration |
| Metabolic syndrome | Dietary and medical management of component disorders, encourage deferral until components adequately managed, consider cardiac stress test, consider transdermal route of administration |
| Severe, refractory or focal migraine* | Consider referral to neurology, consider daily migraine prophylaxis, ensure all other cerebrovascular risk factors are optimized, consider transdermal route of administration |
| Seizure disorder | Consider referral to neurology, consult with a pharmacist re: impact of estrogen interaction with anticonvulsant medication |
| Other cardiac disease | Consider referral to cardiology |
| Hyperprolactinemia | Refer to endocrinology, defer initiation until etiology determined, manage based on etiology |
| History of benign intracranial hypertension | Consider referral to neurology/ neurosurgery |
| Hepatic dysfunction | Dependent on etiology, eg. minimize alcohol consumption, weight loss in NAFLD, consider referral to hepatology/ GI, use transdermal or injectable route of administration |
| Strong family history of breast cancer | Refer to genetics/familial breast cancer program for further risk stratification and BRCA1/2 testing as indicated |
| Personal or Family history of porphyria (rare) | Consider referral to porphyria clinic or internist with experience in porphyria |

* imparts moderate to high risk of an adverse outcome without risk mitigation [40]