**Supplementary Material**

**Preventive drug therapy and contralateral breast cancer: Summary of the evidence of clinical trials and observational studies**

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**Appendix 1. Brief summary of possible side effects of the preventive drugs discussed in the review.**

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| **Drug** | **Possible side effect** | |
| **Type** | **Frequency** |
| **Tamoxifen [1, 2]** | Hot flushes and night sweats  Vaginal discharge and dryness  Low mood  Loss of sex drive  Irregular menstruation | Common |
| Endometrial cancer  Thromboembolic events  Stroke | Less common or rare |
| **Aromatase inhibitorsa [3, 4]** | Nausea  Fatigue  Musculoskeletal complaints  Hot flushes and night sweats  Vaginal discharge and dryness  Low mood  Loss of sex drive  Bone demineralization (may lead to fractures) | Common |
| Hypertension  Hyperlipidemia  Cardiac disordersb | Less common or rare |
| **Bisphosphonatesc [5]** | Nausea  Fatigue  Influenza-like symptoms | Common |
| Oesophageal reactions  Osteonecrosis of the jaw  Renal dysfunction  Hypocalcemia | Rare |
| **Statins [6, 7]** | Myopathy  New-onset diabetes  Hemorrhagic stroke | Very rare |
| **Metformin [8]** | Diarrhea  Nausea  Abdominal discomfort  Lack of energy  Headache  Metallic taste in the mouth | Common /rare |
| **Non-steroidal anti-inflammatory drugs**  **[9, 10, 11]** | Nausea or vomiting  Irritation of the stomach  Gastro-intestinal adverse eventsd Peptic ulcersd  Thrombotic cardiovascular events  Renal adverse events | Common |
| **Anti-hypertensives [12]** | Headache or dizziness  Dry mouth  Cough  Emotional distress or fatigue  Cold hands and feet | Common, but only in mild degree |
| **Fenretinide [13]** | Diminished dark adaptation  Dermatological disorders  Gastrointestinal symptoms  Disorders of the ocular surface | Common, but only in mild degree |

NSAID, non-steroidal anti-inflammatory drug

aMost studies have reported adverse events / side effects for aromatase inhibitors in comparison to tamoxifen.

b The increase in cardiac events observed for AIs compared with tamoxifen is likely due to the cardioprotective effects of tamoxifen.

c Adverse effects vary depending on the type of bisphosphonate prescribed.

d Primarily aspirin and non-selective NSAIDs.

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