which has been shown, in a double-blind randomised placebo-controlled trial, to prevent myocardial infarction and coronary death, albeit with no reduction in overall mortality.

**Fluoxetine in early pregnancy: cardiac birth defects**

- Caution advised with all SSRIs.

In early 2010, the European Medicines Agency reported a meta-analysis of epidemiological studies showing that exposure to fluoxetine in the first trimester of pregnancy is associated with an increased risk of cardiac malformations in newborns (1). The frequency of cardiac malformations was doubled in exposed neonates: 2% versus 1% in the general population.

Concerns about this risk were first raised in 2005, mainly based on troubling population.

- Bevacizumab, sunitinib: osteonecrosis of the jaw
  - Beware invasive dental procedures.

**Bevacizumab and sunitinib** inhibit angiogenesis by blocking the action of vascular endothelial growth factor (VEGF) (1,2). Bevacizumab is an anti-VEGF monoclonal antibody. Sunitinib inhibits the tyrosine kinases linked to the VEGF receptor.

Both of these cancer drugs have been linked to osteonecrosis of the jaw (3,4). The British drug regulatory agency (MHRA) has reported 55 cases of osteonecrosis of the jaw attributed to bevacizumab. They were obtained from the drug company's pharmacovigilance database, which includes clinical trial data and post-marketing reports of adverse drug reactions (3). The French drug regulatory agency (Afssaps) has stated that 27 cases of osteonecrosis of the jaw attributed to sunitinib were reported between 2006 and 2010 (4). The patients had received bisphosphonates, known risk factors for osteonecrosis of the jaw (3). Nevertheless, since bevacizumab and sunitinib inhibit angiogenesis, it is plausible that they played a role in these cases (4).

In practice, this risk should be taken into account by avoiding invasive dental procedures whenever possible, in patients who have been exposed to these drugs, especially when there are other risk factors, such as exposure to bisphosphonates. Dental examination and appropriate preventive dental care should be provided before initiating treatment with these drugs.

**Venous sclerosants: distant ischaemic disorders**

- Dozens of reports.

In 2010, the French National Pharmacovigilance committee examined the results of a survey of ischaemic disorders linked to three venous sclerosants marketed in France: laurromacrogol 400, sodium tetradecyl sulphate, and chrome alum (1,2). The survey was based on spontaneous reports and publications. The disorders included: 12 strokes and transient ischaemic attacks; 35 cases of migraine and visual disorders; 15 cardiac disorders; 8 cases of pulmonary embolism, 7 cases of deep venous thrombosis, and 11 cases of peripheral arterial thrombosis.

Proposed mechanisms include vaso-spasm, or migration of the sclerosant or cellular debris into the pulmonary circulation via the right side of the heart, possibly through a patent foramen ovale (an opening between the right and left atria, present in 20% to 35% of adults).

This is another reminder that local treatments can have significant effects at distant sites.

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**Selected references from Prescrire’s literature search.**
4- Prescrire Rédaction “2-6. Patients ayant une hyperlipidémie” Prescrire 2010; 30 (326 suppl. interactions médicamenteuses).

**Selected references from Prescrire’s literature search.**

**Selected references from Prescrire’s literature search.**
4- Afssaps “Ostéonecrose de la mâchoire chez des patients traités par sunitinib (Sutent®) et ayant reçu précédemment ou de façon concomitante des bisphosphonates” 30 December 2010. afssaps.sante.fr accessed 30 December 2010: 3 pages.