weakness, Passing gas, Seeing, hearing, or feeling things that are not there, Swelling of the breasts or breast soreness in both females and males, Swelling or inflammation of the mouth, and Swollen joints.

(Shoshana J. Herzig et al, 2009).

People who take proton pump inhibitors such as esomeprazole may be more likely to fracture their wrists, hips, or spine than people who do not take one of these medications. The risk is highest in people who take high doses of one of these medications or take them for one year or longer. and in this case they should follow up with a physician (Yu EW *et al.*, 2011).

1.3 Phosphodiesterase 5 inhibitors

1.3.1 General information

PDE5 inhibitors are a group of drugs that are recommended as the first line treatment for the erectile dysfunction (Jardin A, *et al.*, 2000). This group represent mainly three drugs:

- Sildenafil
- Vardenafil
- Tadalafil

Notably they have the same mechanism of action but have some pharmacological differences which lead to different clinical effects (Aytac IA, *et al.*, 1999).

Following sexual stimulation, penile erection occurs through the release of nitric oxide (NO), that causes dilation of the blood vessels of the corpus cavernosum via an accumulation of cyclic guanosine monophosphate (cGMP). PDE5, an enzyme that breaks