

## Omeprazole and erectile dysfunction

### Introduction

Omeprazole is a proton-pump inhibitor for acid-related diseases.

It is registered for use *in benign peptic and duodenal ulcers, reflux esophagitis, severe reflux esophagitis in children above the age of 1 year, treatment of reflux symptoms, acid-related dyspepsia and Zollinger-Ellison syndrome. Beside this, it may be used as prophylaxis in patients, who have to be treated with NSAIDs, but have a medical history of peptic ulcer, erosions or symptoms of dyspepsia.*

Omeprazole is available as capsules (10, 20, and 40 mg), and also as MUPS (Multiple Unit Pellet System) tablets (10, 20, and 40 mg). Omeprazole capsules reached the Dutch market early 1988.

The most common adverse reactions are nausea, vomiting, diarrhoea, constipation, abdominal pain and flatulence, somnolence, sleeping problems, dizziness, headache and paraesthesia [1,2].

### Reports

From 1992 until 1 September 2006, the Netherlands Pharmacovigilance Centre Lareb received 10 reports of erectile dysfunction or impotence in association with omeprazole. The time to onset varied from 1 day to 10 weeks. One patient (patient A) also suffered from decreased libido. In four patients improvement was seen after withdrawal of omeprazole (patient C,D, G, H). In patient F symptoms diminished after a dose reduction to 20 mg daily and treatment with sildenafil. Patient H also suffered from a depression; his medical history included a vasectomy and a hernia nuclei pulposi. In one patient (patient D) a positive rechallenge was observed. Patient C only experienced impotence on a dosage of 20 mg, but not on a lower dosage of 10 mg. He also experienced erectile dysfunction after start of lansoprazole. One patient (patient B) did not recover after discontinuation of omeprazole. Patient E used celiprolol, also known for impotence reaction, as concomitant medication; withdrawal of this drug however did not result in improvement of symptoms.

Table 1. reports of erectile dysfunction/impotence associated with the use of omeprazole

Patient, Sex, age	Report date	Drug Indication for use	Concomitant medication	ADR	Time to onset, outcome
A M, 65	1992	omeprazole 20 mg od not specified	not reported	impotence libido decreased	14 days not reported
B M, 55	1997	omeprazole 20 mg bid gastric ulcer	Tetracycline* Metronidazole* Bismuthcitrate* Cimetidine	impotence	3 days not recovered
C M, 57	1998	omeprazole 20 mg bid diaphragmatic hernia	not reported	impotence	unknown recovered
D M, 46	1999	omeprazole 20 mg bid reflux esophagitis	budesonide betamethasone miconazole	impotence	days recovered
E M, 49	2000	omeprazole 40 mg od not specified	Celiprolol* amlodipine	impotence	10 weeks not reported
F M, 56	2001	omeprazole 40 mg od diaphragmatic hernia	not reported	impotence	1 month recovering
G M, 45	2003	omeprazole 40 mg od dyspepsia	not reported	impotence	2 weeks recovered
H M, 42	2005	omeprazole 20 mg od dyspepsia	not reported	impotence	1 day recovered
I M, 45	2006	omeprazole 10 mg od gastroesophageal reflux	not reported	impotence	3 weeks unknown
J M, 65	2006	omeprazole 20 mg od not specified	colchicines acenocoumarol diclofenac	erectile dysfunction	unknown unknown

\* also indicated as suspect drug

## Other sources of information

### SPC

Erectile dysfunction has not been described in the SPCs of omeprazole capsules and omeprazole MUPS [1,2].

### Literature

Carvajal *et al.* describes three patients who developed impotence, unilateral gynaecomastia or anorgasmia in relation to omeprazol treatment [3]. Another fifteen reports of impotence and fifteen reports of gynaecomastia in association with use of omeprazole were described by Lindquist [4]. Seven of the patients with impotence and five of those with gynaecomastia either had recovered or were improving at the time of notification suggesting a causative role for omeprazole.

## Databases

On 1 September 2006 the Lareb database contained 10 reports of erectile dysfunction or impotence in association with omeprazole, which is not statistically disproportional (ROR 1.87, 95 % CI 0.99-3.51)

On 1 September 2006, the WHO Collaborating Centre had received a disproportional number of 170 reports of impotence in association with omeprazole (ROR 2.13, 95 % CI 1.83-2.48).

## Discussion

The mechanism is not clear. However, in a few publications the influence of proton pump inhibitors on serum free testosterone level was suggested as underlying mechanism for sexual dysfunction. Rosenheim and Flockhart suggest a role for serum free testosterone level in the development of libido loss in a 42-year old woman during treatment with esomeprazole, the S-enantiomer of omeprazole. While taking esomeprazole, the patient's loss of libido improved with oral testosterone supplementation and deteriorated after testosterone withdrawal. There was steady improvement in both sexual function and serum free testosterone concentration after discontinuation of esomeprazole. Due to the temporal relationship between esomeprazole intake and sexual dysfunction, the authors postulate that esomeprazole causes induction of testosterone metabolism. A role of CYP 3A4 had been postulated, converting testosterone to beta-hydroxytestosterone [5].

In the publication of Coulson the influence of lansoprazole treatment on testosterone metabolism and clearance was tested in male rats. Lansoprazole treatment induced hepatic CYP-dependent testosterone metabolism in vitro and enhanced plasma clearance of radio labelled testosterone in vivo. The authors conclude that these effects may have contributed to depletion of circulating testosterone levels [6].

In other publications however no influence of the proton pump inhibitors omeprazole, rabeprazole, pantoprazole or lansoprazole on testosterone plasma levels or other hormones like prolactin was found [7-11].

## Conclusion

Lareb received ten reports of erectile dysfunction in association with omeprazole. In some, a positive dechallenge was observed. Disproportionality in the WHO database supports this association as well as some publications in the literature.

### References

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