CAMPUS GROSSHADERN

HOSPITAL PHARMACY
DEPARTMENT OF UROLOGY

Quality of information on male fertility in the Summary of Product Characteristics (SmPC) - Cause for concern (DI-029)

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Objective

Reasons for male infertility are manifold and often not clearly identifiable. Among others, drug intake can be a contributing factor. A retrospective analysis of 375 male patients wishing to father a child revealed drug consumption in 43,4% (124 different drugs). Access to detailed information on if and how drugs affect male fertility are essential when counselling physicians and patients. According to the European Medicines Agency (EMA) guideline, the Summary of Product Characteristics (SmPC) should include specific information on this topic.

The purpose of this study was to analyse the quality of information in the SmPC regarding the influence of drugs on male fertility.

Methods

SmPCs should contain information on the drugs' impact on male fertility in sections 4.6 – Fertility, pregnancy and lactation and 5.3 – Preclinical safety data. The current German SmPCs of the 124 mentioned drugs were analysed as follows:

- Are required data presented in the appropriate sections?
- Is there a clear distinction between female/male and animal/human data?
- If animal data are presented: is the species given (reproductive cycle duration varies in different test animals/in humans)?

SmPCs were obtained via www.fachinfo.de or the company's website.

Results

The SmPC contain no information on fertility at all in 47 out of the 124 drugs (37.9%). Some mention reproductive studies focused on female reproduction.

Information given in section 4.6:

- General information on the drug's influence on fertility (no distinction between male/female) is presented in 41 SmPCs (33.0%).
- Only 14 SmPCs (11.3%) explicitly provide information on male fertility, referring mainly to data from animal studies.

Information given in section 5.3:

- 82 SmPCs (66.1%) mention reproductive studies regarding fertility (no distinction between male/female) (**Fig. 1**).
- For 17 drugs (13.7%) reproductive toxicity was mentioned.
- Only 10 SmPCs (8,1%) explicitly mention tests on male fertility, 14 (11.3%) refer to male and female fertility and 35 (28.2%) only mention fertility testing without gender distinction (**Fig. 2**).
- Tested animals were detailed in 49 SmPCs (39.6%). Rats, the most common study animals, were listed in 45 SmPCs (91.8%).

In 12 SmPCs (9.7%), additional or the only data on fertility were presented in other sections (not 4.6/5.3).

Cross-reference between 4.6/5.3, as recommended by the European Guidelines, is only given in 29 SmPCs (23.4%).

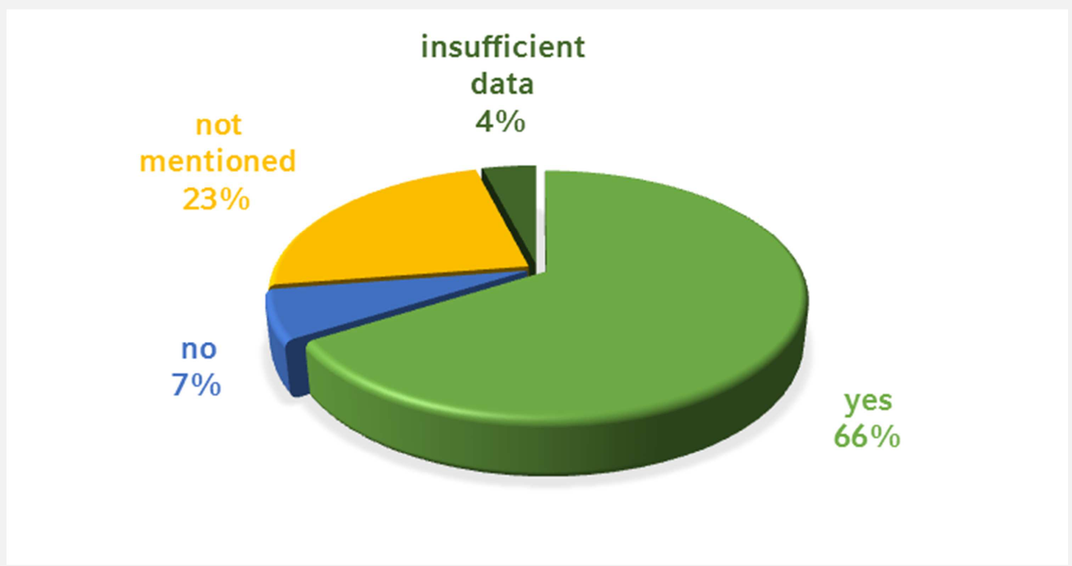

Fig. 1: Reproductive studies on fertility.
Do reproductive studies concerning fertility exist (data from section 5.3)?

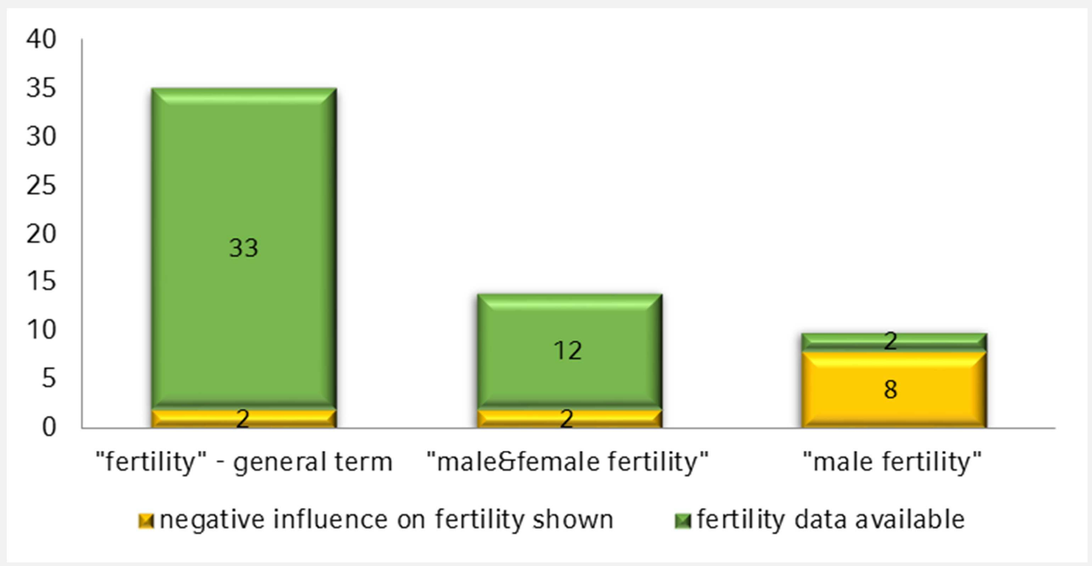

Fig. 2: Fertility data in section 5.3 – Preclinical safety data.
How is information on fertility in section 5.3 distinguished by gender?

Discussion

- Despite the fact that inclusion of information on the impact on fertility in the SmPC is required according to the EMA guideline, almost 38% of the 124 studied SmPCs do not contain any data on this topic.
- Nearly 10% mention fertility data outside the appropriate sections, at least cross-references to/from sections 4.6 and 5.3 would be helpful to locate the information.
- Even SmPC presenting information on fertility issues very often do not distinguish between male and female sex. In many cases it is not obvious if both sexes were tested or are affected.
- Animal data on male fertility are only partly helpful since time for spermatogenesis differs between 35 days in mice, around 40 days in monkeys, and 50 days in rats, while it takes 74 days in men. Therefore, information on the animal species is important but often lacking.

Conclusion

Data on the influence of drugs on male fertility presented in the SmPC are incomplete and in many cases not in line with requirements of the EMA guideline on Summary of Product Characteristics. General statements on „fertility" without distinction male/female are not helpful since reproductive capability of woman and man differs in many aspects.

Literature

Pompe, S.V. et al. Arzneimittelkonsum bei Männern mit unerfülltem Kinderwunsch. J Urol Urogynäkol 2014;21:32-33
European Commission. A Guideline on summary of product characteristics (SmPC). September 2009

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