PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

sanofi

30 May 2023

Important information for healthcare professionals

RE: Clomid 50mg Tablets (Clomifene citrate) - PA 540/20/1

1. **Update to warnings and instructions for use regarding the risk of visual disorders associated in some cases with reversible or permanent/irreversible, partial or total, visual impairment (blindness).**
2. **Introduction of a new contraindication for patients with a history of visual disorders associated with clomifene use.**
3. **Update to visual side effects.**

Dear Healthcare Professional

Sanofi-aventis Ireland Ltd., T/A SANOFI, in agreement with the Health Products Regulatory Authority, would like to inform you of the following important updated safety and prescribing information:

Summary

- **Visual disorders such as blurred vision, reduced visual acuity, phosphenes, optic neuritis, cataract and scintillating scotomas (spots or flashes) are known risks associated with clomifene.**
- **New adverse reactions have been reported during post marketing experience: optic ischaemic neuropathy, central retinal vein occlusion, retinal detachment and vitreous detachment.**
- **Associated symptoms of diplopia, eye pain and accommodation disorders have been included as undesirable effects.**
- **Visual disturbances associated with clomifene are usually reversible. However, these new adverse reactions were associated in some cases with permanent/irreversible, partial or total visual impairment (blindness).**
- **Visual disorders have been observed especially with increased dosage or duration of therapy.**

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Registered in Dublin Ireland No 166500 Directors M. Dempsey (Ireland), U Khan (UK)

- **When starting treatment, patients should be instructed to stop clomifene immediately and inform the physician, if they experience any unusual visual symptoms.**
- **If patients experience visual symptoms, a complete ophthalmological examination is required and the treatment should be permanently discontinued if no other cause of visual disorder is determined.**
- **<u>New Contraindication</u>: Clomifene must not be used in case of a history of significant medically confirmed visual disorder associated with clomifene use (previous or current treatment course).**

Background on the safety concern

Clomifene is approved for:

- Ovulatory failure in women desiring pregnancy

Clomifene citrate is already known to induce ocular and vision disorders. The exact mechanism of visual disorders has not been elucidated.

Cases of optic neuritis, optic ischemic neuropathy, central retinal vein occlusion, retinal detachment, and vitreous detachment have been reported during post-marketing experience (spontaneous reports and literature) with a frequency "rare" in the case of optic neuritis and a frequency "not known" for the other adverse reactions.

These adverse reactions and their associated symptoms "diplopia (double vision), eye pain and accommodation disorders" have been reported as possibly related to the use of clomifene, and have been associated with reversible or permanent/irreversible, partial or total loss of vision (blindness) including after clomifene discontinuation.

The analysis of post marketing cases has not identified any risk factors other than an association in some cases, with treatment for longer duration and higher dosage than recommended. No specific pathological-mechanism has been identified. Therefore, the risk of occurrence and the severity and potential consequences of visual disturbances cannot be anticipated for each case.

Patients should be informed that vision disorders with various visual symptoms can occur. The potential risk of loss of vision should be explained.

Patients should be instructed to stop clomifene immediately and inform their physician whenever any unusual visual symptoms occur.

In such cases, a complete ophthalmological examination is required and the treatment should be permanently discontinued, if no other cause of visual disorders is determined.

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Clomifene must not be used in case of a history of significant medically confirmed visual disorder associated with a previous or current treatment course of clomifene.

The product information has been updated to include:

- instructions/recommendations about the risk of visual disorders associated in some cases with reversible or permanent/irreversible, partial or total, visual impairment (blindness). *(See SmPC sections 4.4: Special warnings and precautions for use; 4.7: Effects on ability to drive and use machines; and 4.8 Undesirable Effects).*

- a new contraindication in case of a history of significant medically confirmed visual disorder associated with clomifene use (previous or current treatment course). *(See SmPC section 4.3: Contraindications).*

The Summary of Product Characteristics (SmPC) and Patient Information Leaflet containing the updated information are available on the HPRA website www.hpra.ie.

This communication has been agreed with the Health Products Regulatory Authority.

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie. Adverse events should also be reported to Sanofi Ireland Ltd. Tel: 01 403 5600. Alternatively, send via email to IEPharmacovigilance@sanofi.com

Company contact point

Should you have any questions or require additional information, please contact Medical Information Department at IEmedinfo@sanofi.com or by phone on 01 403 5600.

Yours sincerely,

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