European Commission

# Titanium dioxide in medicinal products

**Extraordinary Pharmaceutical Committee, 17/9/2021**

Health and Food Safety

# OUTLINE

- **Legal context and implications**
- **Main elements of the draft Regulation**
- **Next steps**

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# Legal context & implications (1)

- **Food additives and medicinal products: a <u>legal link</u>**
  - Directive 2009/35/EC: use of colours in human and veterinary medicinal products **IF** authorised in Regulation No 1333/2008 on food additives, subject to the compliance with the purity criteria
- **<u>Consequence</u>**: Decision to delete TiO2 from the list of authorised food additives is of paramount importance for their use as a colouring matter in medicinal products

# Legal context & implications (2)

- **Impact** of the removal of titanium dioxide from the list of authorised food additives **on medicinal products**?

- 17 May 2021: EC request to EMA
  - Technical purpose of titanium dioxide in medicinal products, scope and functions
  - Feasibility of alternatives to replace titanium dioxide & impact on quality, safety and efficacy of medicines;
  - Transition period for the phasing out of titanium dioxide in all or specific uses in medicines

- 8 September 2021: Final EMA analysis

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# Main elements of the draft Regulation (1)

- **Ban** the use of titanium dioxide **in food**
- **Maintain** the use of titanium dioxide in **medicinal products, *provisionally***
- Pressure on the pharmaceutical industry to develop alternatives
- Review clause of 3 years

→ ***5 Recitals (14 to 18) and 1 article (Article 3)***

# Main elements of the draft Regulation (2)

## *Recital 14*

Directive 2009/35/EC of the European Parliament and of the Council restricts the use of **colours in human and veterinary medicinal products** to those authorised in accordance with Regulation (EC) **No 1333/2008 on food additives**, for which specifications are laid down in Commission Regulation (EU) No 231/2012. **Uses of excipients other than colours in medicinal products** are subject to the Union rules on medicinal products and are evaluated as part of the overall benefit risk profile of a medicinal product.

# Main elements of the draft Regulation (3)

## ***Recital 15 :*** Main conclusions of EMA analysis

- **Widely used** as excipient in **essential medicines** (oral solid and semi-solid dosage forms)
- Mainly used as a **colour and opacifier** - **multiple functions**
- **Alternatives possible** from a **technical point** of view; BUT **feasibility not confirmed** (impact on quality, safety and efficacy of medicinal products)
- **Difficult** at this stage to recommend a **precise transition period timeframe for replacement** of titanium dioxide
- **Global dimension** and impact on **availability**

# Main elements of the draft Regulation (4)

***Recital 16 : use in medicinal products remains possible provisionally***

On the basis of the EMA scientific analysis, and in order to avoid shortages of medicinal products that could have impacts on public health, titanium dioxide (E 171) **should remain provisionally on the list of authorised additives** to allow its use in medicinal products as a colour, pending the **development of adequate alternatives** to replace it while **ensuring the quality, safety and efficacy** of the medicinal products concerned.

# Main elements of the draft Regulation (5)

## Recital 17 : obligations on the pharmaceutical industry

It is of critical importance that the pharmaceutical industry **makes any possible efforts to accelerate the research and development of alternatives** that would be used as a replacement for titanium dioxide (E 171) in medicinal products, and to **submit the necessary variation** to the terms of the marketing authorisations concerned.

**In the absence of such efforts**, competent authorities may request the concerned stakeholders to submit **objective and verifiable reason explaining the non-feasibility** of the replacement.

# Main elements of the draft Regulation (6)

## Recital 18 and Article 3 – Review clause of 3 years

- Commission **committed to review** the necessity **to maintain titanium dioxide (E 171) or otherwise delete** it from the Union list of food additives for exclusive use as a colour in medicinal products within **three years after the date of entering into force** of this Regulation.

- **Updated EMA assessment by 1st April 2024** – Progress made to develop alternatives in new and already authorised products, împact on quality, safety, efficacy & availability

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# Next steps

- 14/09: Working Group on Food Additives
- 17/09: Pharmaceutical Committee
- 28/09: Standing Committee
- European Parliament and Council Scrutiny: 2 months
- COM adoption procedure
- January 2022: Adoption and publication