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Questions and answers on the potential off-label use of celecoxib in patients with familial adenomatous polyposis

Outcome of a procedure under Article 5(3) of Regulation (EC) 726/2004[1]

The European Medicines Agency has completed a review of the use of celecoxib for reducing the number of polyps in patients with familial adenomatous polyposis (FAP). The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that, in view of the dose-related risks, the currently available evidence of efficacy is insufficient to support a recommendation for use of celecoxib in FAP patients.

What is celecoxib?

Celecoxib is a 'non-steroidal anti-inflammatory drug' (NSAID) that belongs to the group 'cyclo-oxygenase 2 (COX-2) inhibitors'. This means that it blocks the COX-2 enzyme, resulting in a reduction in the production of prostaglandins, substances that are involved in the inflammation process.

Celecoxib is currently authorised under various trade names in EU Member States for the treatment of the symptoms of osteoarthritis (swelling and pain in the joints), rheumatoid arthritis (an immune system disease causing damage and inflammation in the joints) and ankylosing spondylitis (a disease causing inflammation of the joints of the spine).

Why was this medicine reviewed?

Celecoxib, under the trade name of Onsenal, received an EU-wide marketing authorisation in October 2003 for the reduction in the number of polyps in patients with FAP. FAP is a genetic disease that causes 'adenomatous intestinal polyps', growths that project from the lining of the colon or rectum (large intestine). These polyps can become cancerous.

Onsenal was used in addition to surgery (to remove the polyps) and endoscopic monitoring (to check if polyps are developing, using an endoscope, a thin tube that allows a doctor to look inside the gut). Onsenal had been authorised under 'exceptional circumstances' because FAP is a rare disease and it had not been possible to obtain complete information on the medicine's benefits and safety. Additional studies to confirm a positive benefit-risk profile were still awaited.

[1] Article 5(3) of Regulation (EC) 726/2004, opinion on any scientific matter concerning the evaluation of medicinal products for human use.

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In March 2011 the company for Onsenal, Pfizer Limited, voluntarily withdrew its marketing authorisation in the EU because it was unable to provide the required confirmatory data on the benefits of the medicine.

Despite the withdrawal of the marketing authorisation for Onsenal, the European Commission was concerned over a possible off-label use of other celecoxib-containing medicines, which have been authorised via national procedures. It therefore requested the CHMP to issue an opinion on the benefit-risk balance of using celecoxib for the reduction in the number of polyps in patients with FAP, in addition to surgery and endoscopic monitoring.

Which data has the CHMP reviewed?

The CHMP looked at the available data on the use of celecoxib in FAP patients. This included the results from the main study that supported the marketing authorisation for Onsenal, an ongoing study with celecoxib, post-marketing safety data and data from the published literature.

What are the conclusions of the CHMP?

The CHMP noted that no relevant additional data on the efficacy of celecoxib have become available to support the limited evidence of the benefits seen in the main study with celecoxib. In particular, there was no evidence that celecoxib reduced the risk of intestinal cancer or the need for surgery. The CHMP therefore concluded that the benefit of celecoxib in FAP patients had not been sufficiently demonstrated.

Regarding the safety of celecoxib in FAP patients, the Committee noted that, although safety data are still limited in these patients, a large amount of data exists for other indications. This includes cardiovascular side effects (such as heart attacks) and gastrointestinal side effects (such as perforations, bleeding and intestinal perforation). Because high-dose long-term treatment was used in FAP patients, the CHMP concluded that the overall increase in the risk of side effects would not be outweighed by the uncertain benefit of the medicine in these patients.

Therefore the CHMP concluded that the existing evidence of safety and efficacy does not support the use of celecoxib in FAP patients.

What are the recommendations for patients and prescribers?

- Doctors and patients are reminded that celecoxib is not authorised for use in FAP patients in the EU.
- Doctors and patients are also reminded that, when celecoxib is used in high doses and for long periods of time for treating FAP, there are known serious risks for patients while its benefits remain uncertain.
- Patients who have any questions should speak to their doctor or pharmacist.

What will happen next?

The CHMP opinion will be communicated to the Member States, so that they can take appropriate action at national level.