EDITORS' OPINION

EMA turns a blind eye to denosumab's lack of proven clinical efficacy

In the absence of a better alternative, one can of course use a drug known to carry a risk of serious adverse effects, provided that this is a fully-informed decision, and that the clinical benefits are significant and very clearly demonstrated. In other words, that the harm-benefit balance is favourable in the clinical setting in question.

Denosumab at a dosage of 60 mg has been marketed in France since 2012. It carries a risk of numerous adverse effects, in particular infections, cancer, hypersensitivity reactions, osteonecrosis of the jaw and external auditory canal, multiple vertebral fractures after discontinuation of the drug, serious, even fatal, hypocalcaemia, and auto-immune disorders.

The European Medicines Agency (EMA) issued a favourable opinion regarding extension of the authorisation for this drug to prevention of osteoporosis caused by long-term corticosteroid therapy. As a result of this opinion, this indication was added to its marketing authorisation (MA) (see "Denosumab (Prolia) and steroid-induced osteoporosis" p. 95). In light of its already extensive profile of known adverse effects, one would expect that its evaluation in the prevention of corticosteroid-induced osteoporosis would be particularly robust and based on clinical criteria that are useful for patients. However, detailed analysis of the evaluation shows that it falls short of the mark: only a single trial has assessed the effect of *denosumab*, with a radiological criterion as the primary outcome measure and no proof of clinical efficacy.

How is it possible that the EMA gives more weight to hypothetical clinical benefits than to serious, well-recognised clinical adverse effects? What kind of blinkers is the EMA wearing that prevent it from seeing the patients lying by the side of the road? (see "New drugs: the right to know" p. 87).

Prescrire

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Volume 40 N° 435 • Page 4

Quality of information from pharmaceutical companies

In response to our systematic requests


Company provided detailed information including unpublished data and packaging items.


Company provided information limited to published administrative data or packaging items.


Company provided minimal information, mainly administrative and packaging items.


Company provided no information.

PRESCRIRE'S RATINGS

Our judgement is based on the therapeutic advance of the new product. It considers not only the inherent value of each product in terms of its harm-benefit balance, but also its advantages and disadvantages relative to existing products available in France. Note that the relative value of new products can vary from one country to another.


BRAVO
The product is a major therapeutic advance in an area where previously no treatment was available.


A REAL ADVANCE
The product is an important therapeutic advance but has certain limitations.


OFFERS AN ADVANTAGE
The product has some value but does not fundamentally change the present therapeutic practice.


POSSIBLY HELPFUL
The product has minimal additional value, and should not change prescribing habits except in rare circumstances.


NOTHING NEW
The product is a new substance but with no evidence that it has more clinical value than other substances of the same group. It can be a me-too or a near me-too.


NOT ACCEPTABLE
Product without evident benefit but with potential or real disadvantages.


JUDGEMENT RESERVED
The editors postpone their rating until better data and a more thorough evaluation of the drug are available.