

Annex C
(variation to nationally authorised medicinal products)

Annex I

**Scientific conclusions and grounds for the variation to the terms of
the marketing authorisation(s)**

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for zoledronic acid (indicated for cancer and fractures), the scientific conclusions of the PRAC are as follows:

In view of available data on tubulointerstitial nephritis from the literature, spontaneous reports including in some cases a close temporal relationship and a positive de-challenge, and in view of a plausible mechanism of action, the PRAC is of the view that a causal relationship between zoledronic acid (indicated for cancer and fractures) and tubulointerstitial nephritis is at least a reasonable possibility. The PRAC concluded that the product information of products containing zoledronic acid (indicated for cancer and fractures) should be amended accordingly.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for zoledronic acid (indicated for cancer and fractures) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing zoledronic acid (indicated for cancer and fractures) is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.

Annex II

**Amendments to the product information of the nationally
authorised medicinal product(s)**

Amendments to be included in the relevant sections of the Summary of Product Characteristics (new text **underlined and in bold**, deleted text ~~strike through~~)

- Section 4.8

The following adverse reaction(s) should be added under the SOC 'Renal and urinary disorders' with a frequency 'Not known':

Tubulointerstitial nephritis

Amendments to be included in the relevant sections of the Package Leaflet (new text **underlined and in bold**, deleted text ~~strike through~~)

- Section 4. Possible side effects

[...]

Tell your doctor about any of the following side effects straight away:

[...]

Not known: frequency cannot be estimated from the available data

- **Inflammation of the kidney (tubulointerstitial nephritis): signs and symptoms may include decreased volume of the urine, blood in the urine, nausea, feeling generally unwell**