

Clcr = creatinineklaring

| Onderbouwend | Bewijs | Effect | Opmerkingen |
|--------------|--------|--------|-------------|
| -            |        |        |             |

| Overig                                                                                                                                                    | Opmerkingen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SPC Erivedge 12-7-2013                                                                                                                                    | Op basis van populatie-farmacokinetische analyse van de gecombineerde gegevens van 5 klinische studies leek de nierfunctie geen invloed te hebben op de farmacokinetiek van vismodegib. Derhalve, gebaseerd op de lage excretie van vismodegib via de urinewegen, wordt geen effect van licht tot matig verminderde nierfunctie verwacht.<br>In klinische studie werd geen verhoging vismodegibspiegel of toxiciteit gezien bij doses 3.6x hoger dan aanbevolen (150 mg/dag)                                                                                                                                                                                                                                                                                                                           |
| EPAR Erivedge                                                                                                                                             | The elimination of vismodegib appears to be primarily via hepatic routes. A combined renal/hepatic impairment study is included in the RMP. As a difference in elimination capacity (intrinsic CL) at organ impairment might not be seen in total concentrations but only in unbound concentrations due to the saturable protein binding of vismodegib free concentrations will be determined.<br>Based on the low urinary excretion of vismodegib, mild-moderate renal impairment would not be expected to lead to clinically relevant increases in unbound concentrations of vismodegib. However, severe renal impairment might affect also metabolism and transport, and a warning of caution at severe renal impairment has been implemented in the SmPC.<br>Data will be available in March 2015. |
| clinicaClinicalTrials.gov<br><a href="http://clinicaltrials.gov/show/NCT01546519">http://clinicaltrials.gov/show/NCT01546519</a><br>geraadpleegd 5-8-2014 | Study NCT01546519<br>A phase Ib open-label pharmacokinetics and safety study of the hedgehog pathway inhibitor vismodegib in patients with advanced solid malignancies including hepatocellular carcinoma with varying degrees of renal or hepatic function. This study has been completed. No study results posted                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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|-------------|--|
| Risicogroep |  |
|-------------|--|

## Opmerkingen:

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Clcr < 10 ml/min:

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|                      | Wijziging kinetiek | Actie | Clcr grens | Datum          |
|----------------------|--------------------|-------|------------|----------------|
| Beslissing werkgroep | Onbekend           | Nee   | -          | 6 januari 2015 |