## Anticancer Drug Dosing in Kidney Dysfunction



The International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD) is available on the eviQ website.

> This document is a summary of the key changes to clinical practice as a result of the ADDIKD guideline recommendations.

## Key changes to clinical practice

- Estimated glomerular filtration rate via the Chronic Kidney Dysfunction-Epidemiology Collaboration 2009 equation (eGFR ${ }_{\text {CKD-EpI }}$ ) replaces creatinine clearance via the Cockcroft Gault equation as the preferred method of estimating kidney function in cancer patients. In some clinical situations it may be necessary to use directly measured glomerular filtration rate (mGFR) (e.g. radioisotope measured GFR).
- eGFR ${ }_{\text {CKD-EPI }}$ is recommended to guide the dosing of anticancer drugs whose dose is dependent on kidney function, except in specific clinical situations or specific anticancer drugs (e.g. carboplatin (discussed below), methotrexate (doses $\geq 500 \mathrm{mg} / \mathrm{m}^{2}$ ), cisplatin) where it may be unreliable.
- Standardised categories for kidney dysfunction. This is based on the Kidney Disease Improving Global Outcomes (KDIGO) Chronic Kidney Disease (CKD) categories to guide the kidney dose adjustments of anticancer drugs.


## Where can you find the eGFR $\mathrm{CKD}_{\text {CRII }}$ value?

- eGFR CKD-EPI is automatically reported by Australian pathology labs.
- The consensus recommendation is that Australian pathology laboratories use CKD-EPI 2009 equation (without the race coefficient) when reporting eGFR $\left(\mathrm{mL} / \mathrm{min} / 1.73 \mathrm{~m}^{2}\right)$. This is reflected in the ADDIKD guideline and utilised in eviQ. In 2021 the original equation was refitted without race (ie CKD-EPI 2021). However, to date, this adjustment has not been adopted by either Australian or international nephrology groups in the cancer setting. See ADDIKD guideline for further details.
- Laboratory eGFR CKD-Ep values are reported to an upper limit of 90, displayed as: eGFR $\geq 90 \mathrm{~mL} /$ $\mathrm{min} / 1.73 \mathrm{~m}^{2}$. To manually calculate eGFR $\mathrm{CKD}-\mathrm{EPI}$ the eviQ eGFR ${ }_{\text {CKD-EPI }}$ calculator is recommended. If alternative online calculators are used, ensure the CKD-EPI 2009 equation is utilised to calculate eGFR with serum creatinine in micromol/L.


## CKD-EPI 2009 equation

| Sex | Serum creatinine (SCr) | eGFR ${ }_{\text {cKd-EPI }}$ equation |
| :---: | :---: | :---: |
| FEMALE | $\leq 62 \mathrm{micromol} / \mathrm{L}$ <br> > 62 micromol/L | $\begin{aligned} & \operatorname{eGFR}_{\text {CKD-EPI }}=144 \times(\mathrm{SCr}(\text { micromol } / \mathrm{L}) \times 0.0113 / 0.7)^{-0.329} \times(0.993)^{\text {age }} \\ & \mathrm{eGFR}_{\text {CKD.EPI }}=144 \times\left(\mathrm{SCr}(\text { micromol/L) } \times 0.0113 / 0.7)^{-1.209} \times(0.993)^{\text {age }}\right. \end{aligned}$ |
| MALE | $\leq 80 \mathrm{micromol} / \mathrm{L}$ <br> > $80 \mathrm{micromol} / \mathrm{L}$ | $\begin{aligned} & \operatorname{eGFR}_{\text {CKD-EPI }}=141 \times(\mathrm{SCr}(\text { micromol/L }) \times 0.0113 / 0.9)^{-0.411} \times(0.993)^{\text {age }} \\ & \operatorname{eGFR}_{\text {CKD-EPI }}=141 \times(\mathrm{SCr}(\text { micromol/L }) \times 0.0113 / 0.9)^{-1.209} \times(0.993)^{\text {age }} \end{aligned}$ |

## ADDIKD recommendations for calculating carboplatin doses:

- Directly measured glomerular filtration rate (mGFR) is the preferred kidney function value in the Calvert formula, especially in patients with either:
- curative treatment intent
- clinical situations where estimated kidney function may be unreliable for accurate therapeutic dosing such as:
- eGFR > $125 \mathrm{~mL} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$
- eGFR $\leq 45 \mathrm{~mL} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$
- extremes of body size or muscle mass
- amputees
- paraplegics
- In all other clinical situations, eGFR adjusted to an individual's body surface area (BSA-adjusted eGFR) is a suitable alternative to directly mGFR for use in the Calvert formula:
BSA-adjusted eGFR CKD-EPI $(\mathrm{mL} / \mathrm{min})=\left[e G F R_{\text {CKD-EPI }}\right.$ $\left.\left(\mathrm{mL} / \mathrm{min} / 1.73 \mathrm{~m}^{2}\right) \times \mathrm{BSA}\left(\mathrm{m}^{2}\right)\right] / 1.73$
* BSA can be calculated using Mosteller or Dubois Dubois formulas


## Note:

If an eGFR value is reported as eGFR $\geq 90 \mathrm{~mL} /$ $\mathrm{min} / 1.73 \mathrm{~m}^{2}$ then manual calculation using serum creatinine is required before adjusting result for BSA to then be used in the Calvert formula.

- Recalculation of carboplatin doses at each cycle is unnecessary, except when baseline kidney function (e.g., eGFR) alters by $>20 \%$ or when there is a change in the clinical status of the patient.
- Reduction of target AUC in kidney dysfunction is not recommended, as it may compromise clinical benefit.


## To assist with these calculations eviQ have the following calculators available:

- a new eGFR ${ }_{\text {CKD-EPI }}$ calculator with the option for BSA-adjusted eGFR ${ }_{\text {скd-ер }}$
- carboplatin dose calculator with options for different AUC and kidney function values


## Implementation of the ADDIKD recommendations into eviQ

- The implementation of the ADDIKD drug recommendations into eviQ is a significant undertaking with 700+ protocols and content across the eviQ website to be updated. It requires significant clinical input to ensure rigor and accuracy so that the information is correct and safe to follow.
- eviQ is working to update all protocols and will provide further details on the timeline of the changes as soon as possible.

For further information please visit the dedicated eviQ ADDIKD webpage.

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