Brand Name: Recarbrio
Generic: imipenem, cilastatin, relebactam
Type: small molecule
Year Accepted/Phase: 2019

Mechanism:

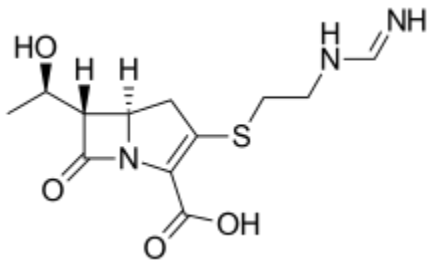
Imipenem: Imipenem is a broad-spectrum beta-lactam antibiotic of the carbapenem class. It works by inhibiting bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), leading to cell lysis and death.

Cilastatin: Cilastatin is a renal dehydropeptidase inhibitor. It inhibits the enzyme dehydropeptidase I, which is present in the kidneys and metabolizes imipenem. By preventing the degradation of imipenem, cilastatin ensures that adequate levels of imipenem are maintained in the body for effective antibacterial action.

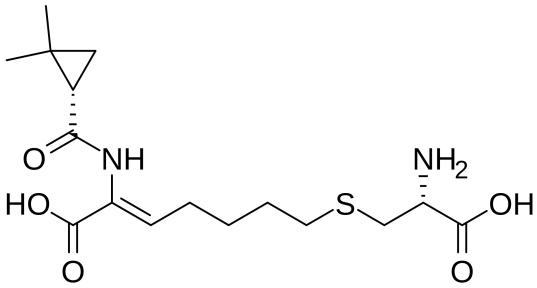
Relebactam: Relebactam is a beta-lactamase inhibitor. It inhibits certain beta-lactamase enzymes produced by bacteria that can hydrolyze and inactivate imipenem. By inhibiting these enzymes, relebactam restores and enhances the activity of imipenem against beta-lactamase-producing resistant bacteria.

Chemical Structure:

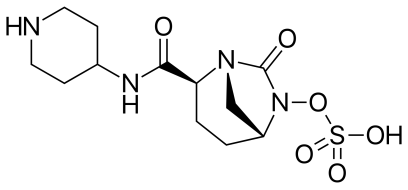
Imipenem



Cilastatin



Relebactam



Indication:

Recarbrio is indicated for the treatment of the following infections in adults who have limited or no alternative treatment options:

Complicated urinary tract infections (cUTI), including pyelonephritis.

Complicated intra-abdominal infections (cIAI).

Hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP).

Clinical trials:

RESTORE-IMI 1 (Phase III)
Pubmed: https://pubmed.ncbi.nlm.nih.gov/31400759/
Purpose: Evaluate the efficacy and safety of imipenem/cilastatin/relebactam versus imipenem/cilastatin plus colistin in treating imipenem-non-susceptible bacterial infections.
Dates: Conducted from 2016 to 2018.
Results: The trial showed that the imipenem/cilastatin/relebactam combination was non-inferior to imipenem/cilastatin plus colistin in terms of clinical response at day 28. It also demonstrated a lower incidence of nephrotoxicity compared to the colistin regimen.
Impact: These results supported the approval of Recarbrio for the treatment of cUTI and cIAI caused by susceptible organisms, offering a safer alternative with reduced nephrotoxicity.

RESTORE-IMI 2 (Phase III)
Pubmed: https://pubmed.ncbi.nlm.nih.gov/32785589/
Purpose: Assess the efficacy and safety of imipenem/cilastatin/relebactam in treating hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia.
Dates: Conducted from 2017 to 2019.
Results: The study demonstrated that the imipenem/cilastatin/relebactam regimen was non-inferior to piperacillin/tazobactam in terms of clinical cure rates and all-cause mortality at day 28. The safety profile was consistent with previous studies, showing a lower incidence of adverse renal effects.
Impact: This trial's findings supported the expansion of Recarbrio's indications to include HABP and VABP, providing an effective treatment option for these serious infections.