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Medication Policy Manual

Policy No: dru178

Topic: Afinitor[®], everolimus

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Revised/Effective Date: May 8, 2009

Next Review Date: May 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Everolimus (Afinitor[®]) is an oral medication used to treat kidney cancer. It works by blocking the growth of cancer cells.

Policy/Criteria

- I.** Most contracts require prior authorization approval of everolimus tablets prior to coverage. Everolimus tablets may be considered medically necessary in patients with renal cell carcinoma (RCC) when prescribed by an oncologist when either sorafenib or sunitinib have not been effective.

- II.** Administration, Quantity Limitations, and Authorization Period
 - A.** Regence considers everolimus tablets to be a self-administered medication.
 - B.** When prior authorization is approved, up to 30 everolimus 5 mg or 10 mg tablets may be authorized per month. Quantities exceeding 30 tablets per month are considered not medically necessary.
 - C.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

- III.** Everolimus tablets are considered investigational when used for all other conditions, including, but not limited to:
 - A.** Allograft rejection after solid organ transplant (eg. lung, kidney, heart).
 - B.** Breast cancer.
 - C.** Colorectal cancer (CRC).
 - D.** Crohn's disease (CD).
 - E.** Gastric cancer.
 - F.** Glioblastoma.
 - G.** Hepatocellular carcinoma (HCC).
 - H.** Neuroendocrine tumors.
 - I.** Tuberous sclerosis.

Position Statement

Summary

- Everolimus (Afinitor[®]) is an orally administered inhibitor of mTOR, a protein kinase that helps to regulate cell division.
- Everolimus (Afinitor[®]) may be an option in patients with advanced renal cell carcinoma (RCC) whose disease has progressed while receiving treatment with sorafenib (Nexavar[®]) or sunitinib (Sutent[®]).
- To date, everolimus (Afinitor) has only been studied after other therapies for advanced RCC have been ineffective.
- The potential for slowing tumor growth must be weighed against the risk of adverse effects.

Efficacy

- A single study compared everolimus (Afinitor) with placebo (best supportive care) in patients with advanced renal cell carcinoma. ^[1, 2]
 - * Patients enrolled in the trial had progression of their disease while on treatment with sorafenib (Nexavar) or sunitinib (Sutent) or both medications given sequentially.
 - * Progression-free survival (PFS), a measure of tumor size using x-rays, was the primary endpoint of the study.
 - * Everolimus (Afinitor) improved PFS by a median of 3 months when compared with placebo.
- There are sufficient flaws in the everolimus (Afinitor) study that may make interpretation of the results unreliable.
 - * More people dropped out of the study in the everolimus (Afinitor) treatment group than the placebo group. This difference exceeded 10% which has the potential to affect the study results. The main reason people left the everolimus (Afinitor) group was because of adverse events.

- * Because crossover to everolimus (Afinitor) was allowed after tumor progression was detected in the placebo group, the overall survival information reported from this trial is not reliable. This means it is uncertain whether treatment with everolimus (Afinitor) helps people live longer.

Safety

- Common (incidence > 30%) adverse reactions with everolimus (Afinitor) include: stomatitis (mouth sores), infections, asthenia, fatigue, cough, and diarrhea. ^[1]
- Non-infectious pneumonitis may occur with everolimus (Afinitor). ^[1]
- Elevations in lipids and blood glucose, and bone marrow suppression are also commonly reported. ^[1]
- There is a high potential for clinically significant drug-drug interactions with everolimus (Afinitor). ^[1]
 - * Everolimus (Afinitor) may slow the metabolism of medications that are processed by the CYP3A4 and CYP2D6 enzyme pathways.
 - * Inhibitors (eg. aprepitant, ketoconazole, erythromycin, verapamil) and inducers (eg. rifampin, dexamethasone) of CYP3A4 and PgP may increase or decrease everolimus (Afinitor) blood concentrations, respectively.

Administration and dosing

- The recommended dose of everolimus (Afinitor) is 10 mg orally daily until disease progression or unacceptable toxicity occurs. ^[1]
- Dose reductions (5 mg orally daily) or interruption of therapy may be used to manage severe and/or intolerable side effects or lab abnormalities (eg. elevated liver enzymes). ^[1]
- Pharmacokinetic studies suggest that an increased dose of everolimus (Afinitor) may be necessary when given concomitantly with CYP3A4 inducers. Avoiding concomitant use of these agents is preferred when possible. ^[1]

Use of sorafenib in other conditions

- Everolimus has been studied in prevention of allograft rejection after solid organ transplant (liver, lung, heart and kidney).^[4-8]
 - * Most of these trials were exploratory enrolling small numbers of patients.
 - * Doses used in these trials are lower (1 to 3 mg/day) than doses approved for treatment of advanced RCC (10 mg/day).
 - * None of the trials was designed to show that everolimus is superior to similar medications currently used to prevent allograft rejection after solid organ transplant [tacrolimus (Prograf[®]), sirolimus (Rapamycin[®]) and mycophenolate (CellCept[®])].
- A study of everolimus in Crohn's disease failed to show a benefit with this treatment.^[9]
- Everolimus is also being studied in many other conditions including: breast cancer, colorectal cancer, gastric cancer, glioblastoma, hepatocellular carcinoma, neuroendocrine tumors, and tuberous sclerosis.^[10] There is no published evidence available for these conditions at this time.

References

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Cross References
Nexavar [®] , sorafenib dru134
Sutent [®] , sunitinib dru128

Codes	Number	Description
HCPCS	J8999	Oral chemotherapeutic drug, not otherwise classified