NEW & APPROVED

Vaccinia Immune Globulin, Atacand

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Vaccinia Immune Globulin Intravenous
(DynPort Vaccine Co.)

An immunoglobulin containing antivaccinia antibody for the treatment and/or modification of serious complications of smallpox vaccination, including eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, and vaccinia infections in people who have skin conditions, such as burns, impetigo, or varicella zoster.

► **Recommended Dosage:** 2 mL/kg administered in an intravenous infusion.

► **Special Considerations:** Adverse effects in two studies of 111 healthy volunteers included headaches, hives, and other types of rashes, but were mild to moderate; overall, vaccinia immune globulin intravenous (VIGIV) was well tolerated.

► **Comment:** Approval of VIGIV—derived from pooled plasma of donors who received booster doses of the approved smallpox vaccine—was based on these studies. In one, serum antibody levels achieved were comparable with those expected with a previously approved intramuscular vaccinia immunoglobulin, but no controlled studies have shown a clinical benefit, such as a reduction in mortality.

The Food and Drug Administration approved VIGIV with the condition that postmarketing studies be conducted, including assessing clinical benefits, such as increased survival in patients with progressive vaccinia and eczema vaccinatum. In a statement, the FDA said the product "may help minimize" the risks of the smallpox vaccine, when used in cases where the vaccine's benefits are thought to outweigh its risks, citing the example of responders to a bioterrorist attack.

Atacand
(candesartan, AstraZeneca)

An angiotensin receptor blocker (ARB) for treating patients with heart failure (NYHA class II-IV and an ejection fraction of 40% or less), to reduce the risk of death from cardiovascular causes and reduce hospitalizations for heart failure. Previously approved for hypertension. The second ARB approved for heart failure (HF); the first was Diovan (valsartan), approved in 2002 for a narrower indication, NYHA class II-IV heart failure in people who cannot tolerate ACE inhibitors. Being reviewed for use with an ACE inhibitor in treating HF, as backed by an FDA advisory panel last month.

► **Recommended Dosage:** Starting at 4 mg/day, with a target dose of 32 mg once daily, achieved by doubling the dose approximately every 2 weeks, as tolerated.

► **Special Considerations:** In the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity (CHARM) program, three trials comparing Atacand with placebo in HF populations, 4% of those on Atacand had to stop use of the drug because of hypotension, vs. 2% of those on placebo. Hyperkalemia leading to discontinuation occurred in 2.4% of those on Atacand and 0.6% of those on placebo. Patients must be monitored closely during titration because some develop renal insufficiency, hyperkalemia, or hypotension—side effects expected with any drug that affects the renal angiotensin system, said Christopher Granger, M.D., director of the cardiac care unit at Duke University, Durham, N.C.

► **Comment:** This approval reflects findings of one of the three CHARM trials, CHARM-Alternative, which enrolled 2,028 patients with symptomatic heart failure and a left ventricular ejection fraction of 40% or less, who were on standard HF treatments but were intolerant of ACE inhibitors. After a median follow-up of 34 months, the risk of cardiovascular death or HF hospitalization was reduced by 23% in those on Atacand, compared with those on placebo, a highly significant effect.

Supporting the approval were results of CHARM-Added, of more than 2,500 patients with NYHA class II-IV heart failure and ejection fractions of 40% or less, and on an ACE inhibitor. Adding Atacand to standard treatment, including a β-blocker, cut cardiovascular mortality by 15%, compared with placebo. The key findings of the CHARM program were that in patients with left ventricular dysfunction, Atacand cut cardiovascular mortality and hospitalization for HF, "and made people feel better," said Dr. Granger, who was on the executive committee for CHARM. He served as a consultant to AstraZeneca at the meeting of the FDA's Cardiovascular and Renal Drugs Advisory Committee,which unanimously recommended approval of Atacand for use in patients on an ACE inhibitor.

Atacand will be an important new tool for treating heart failure. The challenge for clinicians "is to successfully integrate a fairly complex set of medications for patients with chronic heart failure, including careful titration and monitoring to assure that we achieve the benefits that have been seen in trials, and that we do it safely." ■

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