

DRUG INTERACTIONS FOR GROWTH FACTORS AND HORMONES

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14.1 INTRODUCTION

According to the dictionary, the definition of *growth factor* is any of various proteins that promote the growth, organization, and maintenance of cells and tissues. And, the definition of *hormones* is any of various internally secreted compounds that affect the functions of specifically receptive organs or tissues when transported to them by the body fluids. Many of the proteins discussed in other chapters of this book, such as interferons and cytokines, may also be regarded as growth factors or hormones by these definitions. This chapter will discuss the traditional growth factors, primarily hematopoietic growth factors, and hormones, primarily growth hormones and glucagon.

The clinical applications of biotechnology-derived products began with growth factors and hormones in the 1980s. Two decades later, growth factors and hormones ranked the second and the third, respectively, of the top biologic drugs in terms of the U.S. sales¹ only behind therapeutic monoclonal antibodies. The total sales of growth factors and hormones combined accounted for approximately \$20 billion (about \$10 billion each).

In the growth factor category, epoetin α (recombinant human erythropoietin; rhEPO) approved by the U.S. Food and Drug Administration (FDA) in 1989 represents the first commercially available recombinant growth factor.² Filgrastim (recombinant human granulocyte colony stimulating factor, G-CSF) followed closely with an FDA approval in 1991. Subsequently, improvements to these recombinant human growth factors, by hyperglycosylation in the case of darbepoetin α ^{2,3} and by pegylation in the case of pegfilgrastim⁴⁻⁶ and methoxy polyethylene glycol-epoetin β ,^{7,8} resulted in new generations of recombinant proteins with a longer