Glucocorticoids (GC) are hormones with a wide variety of actions, including profound anti-inflammatory/immunosuppressive effects. Their actions are mediated by an intracellular receptor called the glucocorticoid receptor (GCR). The classical GCR that mediates the hormone response is called GCR alpha. Recently however, many GCR isotypes have been described. A defective GC action has been proposed as an etiopathogenic mechanism for the development of inflammatory/autoimmune diseases. Inadequate GC actions may have multiple causes such as: defective hypothalamic-pituitary-adrenal axis function, GC export from cells, hormone metabolization into inactive compounds and modifications of the GC receptor, among others. In 1995, a dominant negative effect of a GC receptor isotype termed beta was described; starting a still unsolved controversy about the role of GCR ? as an inducer of GC resistance in certain pathological conditions. The present article will review the data about a possible role