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Gliclazide Modified Release

Gliclazide modified release (MR) is a formulation that differs from the conventional release (CR) gliclazide formulation, allowing once-daily administration. The gliclazide MR and CR formulations are equally safe and efficacious.[1-3] We believe that the cost and dose-response relationship of sulphonylureas in general and gliclazide CR in particular, require closer scrutiny.

The plasma gliclazide concentration versus time profile of gliclazide MR has been reported to "mirror the glycaemic profile of type 2 diabetic patients".[4-6] However, this does not translate into superior blood glucose-lowering efficacy or improved safety profile when compared with gliclazide CR.[7-11] Therefore, despite pharmaceutically different release profiles, gliclazide MR and CR are therapeutically equivalent (with respect to safety and efficacy). This finding is not surprising as studies on sulphonylureas have found no direct relationship between drug plasma concentrations and blood glucose lowering effect.[12,13]

Various investigators[14-23] have described maximum blood glucose lowering effects of sulphonylureas, including gliclazide, at therapeutic doses approximately half that of the maximum manufacturers recommended dose. Shaw et al.[23] found that increasing the dosage of gliclazide CR to 160 mg/day during long-term administration in type 2 diabetic patients did not lead to greater hypoglycaemic effect. DeFronzo[15] suggested that if no hypoglycaemic effect is observed with half of the maximally recommended dose, further dose increases may not have a clinically significant effect on blood glucose regulation. Additionally, continuous exposure to high sulphonylurea plasma concentrations has been reported to decrease therapeutic efficacy.[16]

The current trend of employing combination pharmacotherapy to manage type 2 diabetic patients may also suggest that for patients requiring >160 mg/day of gliclazide CR (equivalent to 60 mg/day of gliclazide MR), the addition of a second oral hypoglycaemic agent, for example metformin, may be therapeutically logical.

A potential advantage of gliclazide MR over the CR formulation is its once-daily administration at all recommended dosages,[7] whereas gliclazide CR is given once daily for dosages of 80 and 160 mg/day, and in two divided doses for dosages of 240 and 360 mg/day.[24] The once-daily dose administration of gliclazide MR may promote optimal compliance. However, it must be noted that not all patients are noncompliant to twice-daily regimens, and not all patients require dosages of gliclazide CR >160 mg/day.[23]

Gliclazide MR is approximately three times more costly when compared with generic gliclazide CR (manufacturer's price list). However, for patients requiring >160 mg/day of the gliclazide CR preparation, and who are poorly compliant on twice-daily regimens as compared with once-daily regimens, the initial greater cost of gliclazide MR may be offset by the possible benefits gained from improved glycaemic status conferred by the improvement in compliance. However, in lieu of the dose-response relationship discussed earlier,[14-23] dosages of gliclazide CR >160 mg/day may not confer additional clinical benefit. Therefore, the advantage of improved compliance with once-daily dose administration of gliclazide MR may also hold for dosages of gliclazide CR ≤160 mg/day, which is also given once daily.

Since gliclazide MR and gliclazide CR are therapeutically equivalent, the greatest motivation for the use of gliclazide MR over gliclazide CR is its once-daily administration, which may have a beneficial effect on compliance. There is evidence suggesting that dosages of CR gliclazide >160 mg/day may not confer additional clinical benefit. Since CR glicla-

zide dosages ≤160 mg/day are given once daily, the need for the MR formulation is contentious.

It is recommended that the dosages of sulphonylureas in general and gliclazide in particular be reviewed through postmarketing surveillance and the cost : benefit ratio should dictate the choice of the gliclazide product.

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