may also be administered intravenously. That used with animal-source insulins. If an adjustment is needed, it may result in the need for a change in dosage. Some patients taking human insulin may require a change in dosage from animal-source insulin may result in the need for a change in dosage.

Transferring a patient to another type or brand of insulin should be done in the same manner. It is important to consider the patient's overall health and the response to the insulin therapy. If a patient is changing from one type of insulin to another, the injection site should be changed. The site should not be used more than once a month. It is important to inject the insulin at the same site each time.

Huminsulin® R is a rapidly acting insulin preparation.

Therapeutic indications
For the treatment of patients with diabetes mellitus who require insulin for the maintenance of glucose homeostasis.

Posology and method of administration
The dose should be determined by the physician, according to the requirement of the patient. Huminsulin® R should be given subcutaneously, intramuscularly or intravenously. Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month. The injection site should be rotated to the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month. The injection site should be rotated to the upper arms, thighs, buttocks, or abdomen.

Contraindications
Hypersensitivity to Huminsulin® or to any of the formulation excipients, unless used as part of a desensitisation programme.

Under no circumstances should any Huminsulin® formulation other than Huminsulin® R be used as part of a desensitisation programme.

Special warnings and special precautions for use
Transferring a patient to another type or brand of insulin should be done under medical supervision. Changes in strength, brand, manufacturer, type (soluble, isophane, lente, etc.), species (human, human insulin analogues, and/or method of manufacture (recombinant DNA, animal-source insulins) may result in the need for a change in dosage. Some patients taking human insulin may require a change in dosage from that used with animal-source insulins. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

A few patients who experienced hypoglycaemic reactions after transfer to human insulin have reported that the early warning symptoms were less pronounced or different from those experienced with animal insulins. Patients whose blood glucose is greatly improved, e.g. by intensified insulin therapy, may lose some or all of the early warning symptoms of hypoglycaemia and should be advised accordingly.

Other conditions which may make the early warning symptoms of hypoglycaemia different or lost pronounced include long duration of diabetes, diabetic nerve disease, or medications such as inborn blockers. Uncontrolled hypoglycaemia, and hypoglycaemic reactions can cause loss of consciousness, coma or death.

The use of dosage which may be inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hypoglycaemia and diabetic ketoacidosis, conditions which are potentially fatal.

Treatment with human insulin may cause formation of antibodies, but titres of antibodies are lower than those to purified animal insulins.

Insulin requirements may change significantly in the deceased, parathyroid or thyroid glands in the presence of endocrine or hyperinsulinism. Insulin requirements may increase during illness or emotional disturbances.

Adjustment of insulin dosage may also be necessary if patients change their level of physical activity or change their usual diet.

Combination of human insulin with glipizide: Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of pioglitazone and human insulin is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Interactions with other medicinal products and other forms of interaction
Some medicinal products are known to interact with glipizide. The physician should take possible interactions into account and ask patients about their other medications in addition to human insulin (see also section Special warnings and special precautions for use).

Insulin requirements may be increased by substances with hypoglycaemic activity, such as glucocorticoids, thyroid hormones, growth hormones, dexamethasone, beta-2-sympathomimetics (such as terbutaline, salbutamol, terbutaline), thiazides. Insulin requirements may be reduced in the presence of substances with hypoglycaemic activity, such as oral hypoglycaemic agents (OMAs), taken concomitantly with insulin (for example, acetylsalicylic acid), certain antiprion agents (monomeric antibodies, certain angiotensin converting enzyme (ACE) inhibitors [perindopril, enalapril], angiotensin II receptor blockers, non-selective beta-blocking agents and alcohol.

Somatostatin analogues (octreotide, lanreotide) may both decrease and increase insulin requirements.

Fertility, pregnancy and lactation
It is essential to maintain good control of the insulin treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the preconception period and increase during the second and third trimesters. Patients with diabetes who are lactating may require adjustments in insulin dose and/or diet.

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Effects on ability to drive and use machines
The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take appropriate precautions to avoid hypoglycaemia while driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

Unfavorable effects
Hypoglycaemia is the most frequent unfavorable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, coma or death. No specific frequency of hypoglycaemia is present, since hypoglycaemia is a result of both the insulin dose and other factors (e.g. patient's level of diet and exercise).
The pharmacokinetics of insulin do not reflect the metabolic action of that hormone. Therefore, it is more appropriate to examine glucose utilization curves (as discussed above) when considering the activity of insulin.

Preclinical safety data
Huminsulin® is human insulin produced by recombinant technology. No serious acute or subacute toxicological studies have been reported in subhuman toxicology studies. Human insulin was not mutagenic in a series of in vitro and in vivo genetic toxicity assays.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmaco-therapeutic group: Huminsulin® Soluble A10A B01.

PHARMACEUTICAL PARTICULARS
Pharmacodynamic properties
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