SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

INN: Recombinant Human Growth Hormone for Injection

Trade name: Ansomone

2. Qualitative and quantitative composition

2.1 Active substance(s)

Recombinant Human Growth Hormone

2.2 Composition per unit dosage form

Each vial contains 4 international units (1.33mg) Recombinant Human Growth Hormone.（4 IU/vial）.

2.3 Excipients

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Lyophilized powder injection

4. Clinical particulars

4.1 Therapeutic indications

1. Ansomone® is indicated for the growth failure of children due to endogenous growth hormone deficiency (GHD).

2. Ansomone® is indicated for short stature in children caused by Noonan syndrome.

3. Ansomone® is indicated for short stature or growth disorders in children caused by SHOX gene defect.

4. Ansomone® is indicated for short stature in children caused by achondroplasia.

5. Ansomone® is indicated for short bowel syndrome in adults receiving nutritional support.

6. Ansomone® is indicated for treatment of severely burned patients.

4.2 Posology and method of administration

When reconstitution, 1ml sterile water for injection should be injected along the bottle wall, then swirl the vial with a gentle rotary motion until the contents are completely

dissolved, do not shake violently.

4.3 Contraindications

1. Ansomone® should not be used in patients whose epiphysis had been closed.

2. Ansomone® should not be used in patients in acute shock stage with severe infection.

3. Ansomone® should not be used in patients with known allergy to growth hormone or its protective agents.

4. Ansomone® should not be used in cancer patients with active neoplasia. Any existing malignancy should be inactive and complete tumor treatment prior to growth hormone therapy. GH therapy should be discontinued if evidence of tumor recurrence. Because growth hormone deficiency may be an early sign of the presence of pituitary tumors (or other rare brain tumors), therefore, the presence of such tumors should be excluded before treatment. Growth hormone should not be used in any patients with potential intracranial tumor progression or recurrence.

5. Ansomone® should not be used in patients with complications of the following acute critical diseases: open heart surgery, abdominal surgery, or multiple trauma.

6. Ansomone® should not be used when acute respiratory failure occurs.

7. Ansomone® should not be used in patients with proliferative or severe nonproliferative diabetic retinopathy are contraindicated.

4.4 Special warnings and precautions for use

1. rhGH therapy should be conducted on exactly diagnosed GHD patients under advice of experienced doctor.

2. Impaired glucose tolerance and glycuresis: Monitoring blood sugar levels regularly in all patients treated with growth hormone, especially those with diabetes risk factors, such as obesity, turner syndrome, or a family history of diabetes, and blood glucose levels during growth hormone therapy in patients with type 1 or 2 diabetes or impaired glucose tolerance should be closely monitored. The dosage of antihyperglycemia drugs (such as insulin or oral or injectable drugs) in these patients needs to be adjusted.

3. Hypoadrenia: Patients who were previously diagnosed with adrenal hypofunction and treated with glucocorticoid replacement therapy need to increase the initial or

maintenance dose of growth hormone therapy.

4. Thyroid gland function should be tested regularly because clinical hypothyroidism may occur to some patients during rhGH therapy. For those hypothyroid, thyroid supplementation is necessary for ensuring the therapeutic effects of rhGH.

5. If lameness, hip or knee pain occur during the treatment period of growth hormone, it is necessary to evaluate whether there is slippage of epiphyseal plate of femoral head.

6. Bow legs may worsen in patients with growth hormone therapy for cartilage dysplasia with bow legs. Such patients should be closely observed when taking medicine. If any abnormality is found, the administration should be stopped and appropriate measures should be taken.

7. In the treatment of patients with cartilage hypoplasia with macroporous stenosis by growth hormone, this class of drugs may contribute to the deterioration of symptoms, administration can only be considered when it is judged that the benefit of drugs for improving short stature is greater than the risk of deterioration of spinal stenosis / macroporous stenosis. Regular monitoring, such as MRI, should be fully carried out, and the administration should be promptly stopped when the deterioration of macropore stenosis is observed.

8. In the treatment of short bowel syndrome in adults, tissue swelling (especially swelling of the hands and feet) due to increased fluid retention, musculoskeletal discomfort (pain, swelling and/or stiffness) due to joint pain, and carpal tunnel syndrome may occur. Symptoms of fluid retention and joint pain may generally be relieved by themselves, or analgesic therapy or dose adjustment may be alleviated according to the degree of onset. Stop growth hormone therapy if the dose reduction still unable to relieve carpal tunnel syndrome.

9. Blood glucose may be increased transitorily during the treatment of severe burns, but it could be returned to normal with the continued therapy of rhGH or with additional treatment of insulin. The treatment with rhGH should be stopped while blood glucose level is greater than 11.1mmol/L for over 3 days with additional treatment of insulin.

10. Injection site should often variation in case lipoatrophy.

11. Progression of scoliosis can occur in rapidly growing patients. Because growth

hormone therapy can increase the growth rate, patients with a history of scoliosis should be monitored for scoliosis progression during growth hormone therapy. Growth hormone therapy has not been shown to increase the incidence of scoliosis. Noonan syndrome itself is often accompanied by skeletal abnormalities such as scoliosis. In clinical studies of SHOX gene defects treated with growth hormone, more patients developed scoliosis in the growth hormone treatment group than in the control group (Clinical trial information from the similar product manual approved for marketing abroad). Caution should be given to these abnormalities that may occur during growth hormone therapy.

12. Congenital heart disease is the main manifestation of Noonan syndrome. There is no evidence that somatrophin induces ventricular hypertrophy or exacerbates existing ventricular hypertrophy. Children with Noonan syndrome and severe heart disease should be adequately evaluated before taking growth hormone therapy to determine whether heart disease severity has a significant effect on growth.

13. The size and number of skin nevi, gynecomastia, joint pain, especially in patients with SHOX gene defects, were monitored during treatment. Caution should be given to these abnormalities that may occur during growth hormone therapy.

14. Acute critical illness: There have been reports of increased mortality after somatropin therapy for several reasons, such as open heart surgery, abdominal surgery, multiple accidental trauma, or acute respiratory failure. The safety of continued use of approved doses of growth hormone in patients with these diseases has not been established. Therefore, the potential benefits and risks of continuing somatropin therapy in patients with acute critical illness need to be assessed.

15. Tumors: Childhood cancer survivors treated with craniocerebral radiation for their first tumor have been reported to have an increased risk of developing a second tumor with secondary growth hormone deficiency and growth hormone therapy. Intracranial tumors, especially meningiomas, are the most common second tumors. All patients with growth hormone deficiency secondary to intracranial tumors are routinely monitored for tumor progression or recurrence during growth hormone therapy.

16. Doctors should weigh the risks and benefits of growth hormone therapy in children with short stature who have an increased risk of developing tumors due to a rare genetic mutation. If somatropin therapy has been initiated, attention should be paid to monitoring the development of the tumor.

17. Leukemia: Occurs in a few patients with growth hormone deficiency, some of whom have been treated with growth hormone. But there is no evidence that treatment with somatropin increases the incidence of leukaemia in patients without predisposing factors.

18. Intracranial hypertension: Fundoscopy for papilloedema should be performed routinely prior to the initiation of somatropin therapy to rule out preexisting papillary edema of the optic nerve and should be performed periodically during therapy. If papilloedema is confirmed during therapy, the growth hormone treatment should be discontinued. If the increase in intracranial pressure induced by growth hormone is confirmed, the growth hormone therapy can be resumed at a lower dose after the signs and symptoms related to the increase in intracranial pressure have been relieved.

19. Severe allergy: Patients and caregivers should be informed of the possibility of allergic reactions. If allergic reactions occur, they should be treated in time.

20. Fluid retention: its clinical manifestations (e.g., edema, postoperative myalgia syndrome, nerve compression syndrome such as carpal tunnel syndrome/tactile abnormalities) are transient and dose-dependent.

21. Laboratory examination: Serum levels of phosphorus, alkaline phosphatase, parathyroid hormone, and IGF-1 may be elevated during growth hormone therapy.

22. Pancreatitis: Children treated with growth hormone rarely report pancreatitis, and some evidence suggests that children are at higher risk than adults. Any patients treated with growth hormone, especially children with abdominal pain symptoms, should consider the possibility of pancreatitis.

23. Careful use of athletes.

4.5 Interaction with other medicinal products

- 11 β -Hydroxysteroid dehydrogenase type 1 (11 β -HSD1): In fat and liver tissues, conversion of adrenocortical ketone to active metabolite cortisol requires microsomal enzymes 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1). As endogenous and exogenous growth hormone can inhibit 11 β -HSD1, therefore, the 11 β -HSD1 and blood cortisol of untreated patients with growth hormone deficiency will relatively increase. The treatment with rhGH inhibited 11 β -HSD1 and decreased the concentration of cortisol in the blood. Therefore, patients with previously undiagnosed central (secondary) hypoadrenalinism may develop and be diagnosed

with rhGH therapy and may require glucocorticoid replacement therapy. In addition, patients who have been diagnosed with adrenal dysfunction and are receiving glucocorticoid replacement therapy may require an increase in maintenance or stress doses after initiation of rhGH therapy; especially in patients treated with cortisone acetate and prednisone because these hormones have to rely on 11 β -HSD1 of activity to convert into their bioactive metabolites.

- Pharmacological dose of glucocorticoid therapy and hyperphysiological dose of glucocorticoid therapy: Excessive glucocorticoid therapy can inhibit the actions of hGH. Patients receiving concomitant glucocorticoid therapy should have their dose carefully adjusted, so that hydrocortisone dosage would be lower than 10~15 mg/m2 of body surface during rhGH therapy.

- Non-androgenic steroids: Simultaneous using of non-androgenic steroid during rhGH therapy can accelerate growth rate.

- Drugs metabolized by cytochrome P450 (CYP450): Limited published data shows that, somatropin administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes. The clearance of compounds metabolised by cytochrome P450 3A4 (e.g. sex steroids, corticosteroids, anticonvulsants and cyclosporine) may be increased resulting in lower plasma levels of these compounds. The clinical significance of this is unknown.

- Oral estrogen: Oral estrogen may reduce the response of blood IGF-1 to rhGH therapy, therefore, in women taking oral oestrogens, a higher dose of somatropin may be required to achieve the treatment goal.

- Insulin and/or other hypoglycemic medications: Patients taking insulin for diabetes mellitus should be carefully monitored during treatment with somatropin. Because hGH may induce a state of insulin resistance, an adjustment of the insulin dose.

4.6 Pregnancy or lactation

It is not recommended for pregnant and nursing women to accept rhGH therapy.

4.7Pediatric

Response to rhGH of children is similar to that of adults in pharmacology, toxicology and pharmacokinetics, rhGH is safe for pediatric use.

4.8 Old patients

There are no data on the use of this medicinal product in old patients.

4.10 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, depending on the sensitivity of the individual patient, the medical may have an effect on the speed of reaction which could impair certain operations.

4.11 Undesirable effects

The following information on possible adverse reactions to the use of growth hormone was obtained from the literature data of similar products abroad, including those that occurred in clinical trials and those reported in spontaneous reports after marketing.

Data from foreign clinical trials of growth hormone products: since clinical trials are conducted under different conditions, the incidence of adverse reactions of one type of growth hormone preparation is often not comparable with that of another type, and the incidence of adverse reactions is not reflected in the actual clinical use of the situation.

Growth hormone is a kind of protein medicine that produces antibodies in a few patients. Studies have shown that a small number of patients who have not been treated with somatrophin have developed somatrophin-specific antibodies at concentrations of less than 2 mg/L after 6 months of somatrophin therapy. Long-term injection of recombinant human growth hormone, if produced antibody, but antibody binding force is low, there is no definite clinical significance. However, if the antibody binding force exceeds 2mg/L, the efficacy may be affected. In addition to the evaluation of compliance and thyroid function, any patient who does not respond to growth hormone therapy should be tested for growth hormone antibody.

Children

Growth hormone deficiency

In studies of growth hormone deficiency in children, the following adverse reactions are rare, such as injection site reactions, including injection site pain, swelling, fibrosis, nodules, rashes, inflammation, pigmentation or bleeding; adipose atrophy; headache; hematuria; hypothyroidism; transient mild hyperglycemia; and mild and transient edema.

Noonan syndrome

A prospective, randomized, parallel dose controlled trial for 2 years, 21 patients with Noonan syndrome aged 3-14 years were enrolled. The dosage of the treatment is 0.033 mg/kg/day and a dose of 0.066mg/kg/day, respectively. After completing 2 years of clinical trials, continuous application of growth hormone therapy to lifetime high. There was no difference in adverse events between the two dose groups.

Congenital heart disease is a congenital disease associated with Noonan syndrome, There was no evidence during the study that growth hormone induced ventricular hypertrophy or exacerbated existing ventricular hypertrophy (as determined by B-ultrasound). Children with severe heart disease were excluded from the study before it started, so the safety of growth hormone therapy for children with Noonan syndrome with severe heart disease is unknown. In children who treated with a dose of 0.033mg/kg/day, scoliosis occurred in 1 case; In children who treated with a dose of 0.066mg/kg/day, scoliosis occurred in 4 case. For growth hormone therapy, the average serum 1GF-1 level did not exceed + 1, and the average serum 1GF-1 level was low at baseline, and gradually normalized during the treatment.

SHOX gene defect

A randomised, openness study for 2 years, the adverse reactions related to growth hormone therapy and of clinical significance are shown in Table 1. After 1 year, the average fasting glucose level in the growth hormone group was close to the baseline and within the normal range. None of the patients had diabetes or fasting glucose concentration above the normal range. In the second year of the study, the growth hormone treated group and the untreated group, the proportion of patients whose IGF-1 concentration exceeded the mean of the same age and gender 2SD at least once was 10/27(37.0%) and 0/24(0%), respectively. The proportion of patients whose IGF-3 concentration exceeded the mean of the same age and gender 2SD at least once was 16/27(59.3%) and 7/24(29.2%), respectively.

Table 1: Major adverse reactions in clinical trials with SHOX gene defects a,b

Adverse Reactions	Control Group	Treatment Group
The total number of patients	25	27
Number of patients with at least one event	2	5
Joint pain	2 (8.0%)	3 (11.1%)

Gynecomastia *	0 (0.0)	1 (8.3%)
Excessive skin moles	0 (0.0)	2 (7.4%)
Scoliosis	0 (0.0)	1 (3.7%)

a. All incidents are non-serious.

b. The occurrence of more adverse events in the growth hormone treatment group than in the control group was included.

*. Only the percentage of male patients was calculated (1/12).

Achondroplasia

In a safety assessment study of 46 subjects, 25 patients (54.3%) had side effects of abnormal changes in clinical examination. The main adverse reactions were bow legs deterioration (2 cases: 4.3%), OGTT abnormality (10 cases: 21.7%), eosinophilia (6 cases: 13.0%), HbA1 increase (6 cases: 13.0%). In the safety assessment of 103 subjects using the performance survey, 17 cases (16.5%) had side effects of abnormal changes in clinical examination. The main side effects were atypical lymphocyte increase (3 cases: 2.9%), spinal stenosis (3 cases: 2.9%), increase of CK (CPK) increased (2 cases: 1.9%).

Adult

Short bowel syndrome

In a double-blind, randomized, placebo-controlled clinical trial, 32 patients treatment with growth hormone for 4 weeks. Among the 41 patients enrolled in the trial: 16 patients received growth hormone (0.1 mg/kg/day) + supportive diet; 16 patients received growth hormone (0.1 mg/kg/day) + supportive diet + oral glutamine (30 g/day); 9 patients received placebo + supportive diet + oral glutamine (30g days). More than 20 percent of patients treated with growth hormone alone, the incidence of the most common adverse reactions was higher than that of the control group, including , facial edema, joint pain, injection site pain, gastrointestinal flatulence and abdominal pain (see Table 2 below). After 4 weeks of growth hormone treatment, the patient was discharged from the hospital, continued on a supportive diet with oral supplementation of glutamine or glutamine placebo, and returned to the clinic for reevaluation 12 weeks later. No new adverse drug reactions were found during follow-up.

Table 2: Adverse effects of growth hormone in randomized, placebo-controlled trials in adults with short bowel syndrome

Adverse effects	Treatment Group		
	rhGH n=16 n(%)	rhGH+Gln n=16 n(%)	Placebo+Gln n=9 n(%)
Peripheral edema	11 (69)	13 (81)	1 (11)
Facial edema	8 (50)	7 (44)	0 (0)
Joint pain	7 (44)	5 (31)	0 (0)
Injection site pain	5 (31)	0 (0)	0 (0)
Gastrointestinal flatulence	4 (25)	4 (25)	2 (22)
Abdominal pain	4 (25)	2 (13)	1 (11)
Injection site response	3 (19)	4 (25)	1 (11)
Vomiting	3 (19)	3 (19)	1 (11)
Ache	3 (19)	1 (6)	1 (11)
Nausea	2 (13)	5 (31)	0 (0)

Post-marketing data of foreign growth hormone products: the adverse reactions reported in spontaneous post-marketing reports were from people with uncertain sample size, and the incidence of adverse reactions or their correlation with drug exposure could not be reliably assessed.Therefore, the occurrence of the following adverse reactions may be different in patients with actual use of growth hormone therapy.

Severe allergy: It is very rare and has been reported in the foreign literature that severe systemic allergic reactions, including anaphylaxis and angioneurotic edema, have occurred after therapy.

Nervous system: Headache (common in children, occasional in adults).

Skin: Increased size and number of skin nevi, especially in patients with SHOX gene defects.

Endocrine: Gynecomastia.

Gastrointestinal tract: Pancreatitis.When patients develop abdominal pain, especially in children, it should be considered for pancreatitis.

Metabolism: Some patients have newly developed type 2 diabetes.

Tumor: Leukemia has been reported in a small number of children treated with growth hormone. However, it is not certain whether it is related to the treatment of growth hormone, the pathology of the growth hormone deficiency disease itself or other related treatments (such as radiotherapy).At present, it has not been confirmed that the treatment of growth hormone is related to the leukaemia.

4.11Overdose

1. Acute overdose could lead initially to hypoglycaemia and subsequently to hyperglycaemia.

2. Long term over-dosing could result in signs and symptoms of gigantism and/or acromegaly consistent with the known effects of rhGH excess.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Recombinant human growth hormone (rhGH) is secreted by growth hormone (GH) secreting cells containing eosinophilic granules in the anterior pituitary. It is a peptide hormone composed of 191 amino acids. Recombinant human growth hormone (rhGH) was produced by the highly efficient expression of rhGH gene in escherichia coli. The amino acid content, spatial conformation and sequence of the active substance is identical to that of rhGH of pituitary origin. Ansomone® exerts the same actions of endogenous human growth hormone. It can stimulate proliferation and differentiation of epiphysis chondrocyte, stimulate growth of cartilage matrix cells, stimulate proliferation and differentiation of osteoblast; thus accelerate the liner growth rate and improve epiphysis width. Ansomone® can promote protein synthesis in whole body; reverse the negative nitrogen equilibrium caused by wound and surgery; correct the hypoproteinemia due to severe infection or hepatocirrhosis; stimulate synthesis of immune globin and proliferation of lymphadenoid, macrophage and lymphocyte, thus enhance the ability of infection resistance; stimulate proliferation of collagenocyte, fibroblast and macrophage in sites of burn and surgery, thus accelerate wound healing; promote synthesis of cadiocytes, thus improve cardiac contractility and reduce cardiac oxygen consumption; regulate lipometabolism, thus depress serum cholesterol and

low density lipopretein’ s level; complement insufficiency or deficiency of growth hormone, regulate adult’ s lipomeabolism, osteometabolism, heart and kidney function.

5.2 Pharmacokinetic properties

1. It is reported that the equal pharmacological effect could be achieved via subcutaneous (SC) or intramuscular (IM) administration. Even though SC may lead a higher concentration of GH in plasma, IM could also yield the same IGF-I level. The absorption of GH is the relatively slow, Cmax often occurs at 3-5 hours after injection. Clearance of GH is via liver and kidney, the half-life of clearance is about 2-3 hours. Uncatabolized GH excreted in urea is almost immeasurable. All of the GH in circulation system exists as a complex form with GH binding proteins that make the half-life of GH prolonged.

2. Almost all GH in the circulation binds to the high-affinity GH-binding protein (hGHBP), This compound prolongs the half-life of GH in serum, and the choice of injection time during the day will not affect the serum GH concentration.

There is no study on this item.

5.3 Preclinical safety data

In the long-term toxicity test, they were divided into four dose groups, namely high, medium, low and control groups. 20 healthy female SD rats were divided into high-dose group (financial equivalent to 50 times of the clinical dose of appointment (3.125 mg / kg), medium dose and low-dose group (25 times (1.563 mm / kg) and 8 times (0.500 mg / kg). RHuGH was used for intramuscular injection (IM) for 42 consecutive days（14 days after drug withdrawal, the toxic reaction and recovery of rats were observed. The results showed that the body weight of male and female rats increased in 42 days after administration of high-dose and medium dose rrhGH ($p < 0.05$). In addition, the blood Glu content of high-dose rats increased in 42 days after administration of rhGH ($p < 0.05$). These changes belong to pharmacodynamic effect and can be recovered after 14 days of drug withdrawal. Therefore, it is considered that rhGH is a low toxicity growth promoting drug.

6. Pharmaceutical particulars

6.1 List of excipients

Mannitol

Glycine

Sodium-bicarbonate

Water for injection

6.2 incompatibilities

1. 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) : In fat and liver tissues, conversion of adrenocortical ketone to active metabolite cortisol requires microsomal enzymes 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1). Endogenous and exogenous growth hormone can inhibit 11β-HSD1, therefore, untreated growth hormone deficiency patients with 11β-HSD1 and blood cortisol will be relatively increased. The treatment with growth hormone inhibited 11 β-HSD1 and decreased the concentration of cortisol in the blood. Therefore, patients with previously undiagnosed central (secondary) hypoadrenalinism may develop and be diagnosed with growth hormone therapy and may require glucocorticoid replacement therapy. In addition, patients who have been diagnosed with adrenal dysfunction and are receiving glucocorticoid replacement therapy may require an increase in maintenance or stress dose after initiation of growth hormone therapy; especially in patients treated with cortisone acetate and prednisone because these hormones have to rely on 11 β-HSD1 of activity to convert into their bioactive metabolites.

2. Pharmacological dose of glucocorticoid therapy and hyperphysiological dose of glucocorticoid therapy: Excessive glucocorticoid therapy can inhibit the actions of rhGH. Patients receiving concomitant glucocorticoid therapy should have their dose carefully adjusted, so that hydrocortisone dosage would be lower than 10-15 mg/m2 of body surface during rhGH therapy.

3. Non-androgenic steroids: Simultaneous using of non-androgenic steroid during rhGH therapy can accelerate growth rate.

4. Drugs metabolized by cytochrome P450 (CYP450) : Limited published data shows that, somatropin administration may increase the clearance of compounds known to be metabolised by cytochrome P450 isoenzymes. The clearance of compounds metabolised by cytochrome P450 3A4 (e.g. sex steroids, corticosteroids, anticonvulsants and cyclosporine) may be increased resulting in lower plasma levels of these compounds. The clinical significance of this is unknown.

5. Oral estrogen: Oral estrogen may reduce the response of blood igf-1 to growth

hormone therapy, therefore, in women taking oral oestrogens, a higher dose of somatropin may be required to achieve the treatment goal.

6. Insulin and/or other hypoglycemic medications: Patients taking insulin for diabetes mellitus should be carefully monitored during treatment with somatropin. Because rhGH may induce a state of insulin resistance, an adjustment of the insulin dose.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Keep at 2~8℃ away from light. The reconstituted solution can be stored at 2~8℃ for 48 hours, do not be frozen.

6.5 Nature and contents of immediate package

Tube-type Bottle, 1 vial/box.

6.6 Instructions for use and handling, and disposal

1. The recommended dosage of Ansomone® for the treatment of growth retardation in children due to endogenous growth hormone deficiency is 0.1~0.15 IU/kg/day (0.033~0.050mg/kg/day), subcutaneous administration, once daily. However, the dosage varies from person to person. Treatment course: it is recommended to use until the epiphysis is closed, or modified according to experienced doctor’s suggestion.

2. The recommended dosage of Ansomone® for the treatment of short stature in children caused by Noonan syndrome is 0.1~0.2 IU/kg/day (0.033~0.066 mg/kg/day), subcutaneous administration, once daily. Treatment course: Use until epiphysis is closed is recommended, or modified according to experienced doctor’ s suggestion.

3. The recommended dosage of Ansomone® for the treatment of short stature or growth disorders in children caused by SHOX gene defect is 0.15 IU/kg/day (0.05 mg/kg/day) or 1.05 IU/kg/week (0.35 mg/kg/week), subcutaneous administration. Treatment course: Use until epiphysis is closed is recommended, or modified according to experienced doctor’ s suggestion.

4. The recommended dosage of Ansomone® for the treatment of short stature in children caused by achondroplasia is 0.15 IU/kg/day (0.05 mg/kg/day) or 1.05 IU/kg/week (0.35 mg/kg/week), subcutaneous administration. Treatment course: Use until epiphysis is closed is recommended, or modified according to experienced

doctor’ s suggestion.

5. The recommended dosage of Ansomone® for the treatment of short bowel syndrome in adults receiving nutritional support is 0.3 IU/kg/day (0.1 mg/kg/day), subcutaneous administration, once daily. The maximum daily dose should not exceed 24 IU (8mg). Treatment course: Continuous treatment for 4 weeks is recommended. Fluid retention and arthralgia / carpal tunnel syndrome occurred during treatment, the dosage can be adjusted according to the degree of occurrence: For moderate cases, use analgesics for symptomatic treatment or reduce the recommended dose to 0.15IU/kg (0.05mg/kg), subcutaneous administration, once daily, and the maximum daily dose is 12 IU (4mg); for severe cases, stop using growth hormone for 5 days at most. After the symptoms disappear, inject subcutaneously once a day for 0.15 IU/kg (0.05mg/kg), and repeat the treatment with maximum daily dose of 12 IU (4 mg). If severe cases occur again or do not disappear within 5 days, stop using growth hormone treatment.

6. The recommended dosage of Ansomone® for the treatment of severe burn is 0.2~0.4 IU/kg/day(0.067~0.133 mg/kg/day) subcutaneous administration for 2 weeks.

7. Registration certificate holder

Anhui Anke Biotechnology (Group) Co., Ltd.

Name and location of manufacturer :Anhui Anke Biotechnology (Group) Co., Ltd.

Ankebio Buildings, No. 669, West Changjiang Road, Hefei, China.

8. Registration certificate number

GYZZS19990021

9. Date of the first registration or re-registration of medicinal product

14/10/2020

10. Date of revision of the text of the summary of product characteristics

14/10/2020