Part VI. SUMMARY OF ACTIVITIES IN THE RISK MANAGEMENT PLAN

Products containing Vitamin D have been available in the European Union for more than twenty years. Their use is well established with recognised efficacy and acceptable safety. The chosen level of 800 IU is well within the dose range commonly used in clinical practice.

Vitamin D insufficiency is very common and vitamin D deficiency is fairly common in European countries. A daily dose of 400 IU vitamin D is too often insufficient, while 800 IU more often elevate the serum 25(OH)D to a level of sufficiency. A vitamin D₃ tablet with 800 IU fulfils a clinical need and is safe.

The approved SmPC provides a detailed description of the benefits and risks with colecaciferol 800 IU and no other activities other than routine Pharmacovigilance activities as described in section III are deemed necessary as a risk management plan for Divisun/Colecaciferol Meda 800 IU tablet.

VI.1. ELEMENTS FOR A PUBLIC SUMMARY

VI.1.1. Overview of disease epidemiology

Vitamin D insufficiency is widespread and is present in every region of the world. In elderly populations in Europe, vitamin D insufficiency is more common in the south than in the north, and more likely in women than men. It may be present in as many as half of women suffering from osteoporosis. A number of factors influence the ability to produce vitamin D in the skin and may contribute to the risk of low levels of vitamin D. These factors include variation in sun exposure due to latitude, season, time of day, air pollution, clothing, sunscreen use and skin pigmentation, as well as age, obesity and the incidence of several chronic illnesses. Approximately 30% of all postmenopausal women have osteoporosis in Europe. At least 40% of these women and 15-30% of men will suffer one or more fractures due to osteoporosis in their remaining lifetime. The most common fractures associated with osteoporosis occur at the hip, spine and wrist. Of particular concern are vertebral (spinal) and hip fractures. Vertebral fractures can result in serious consequences, including intense back pain and deformity (sometimes called Dowager's Hump). A hip fracture often requires surgery and may result in loss of independence or death.

VI.1.2. Summary of treatment benefits

Treatment with vitamin D (colecaciferol) cures osteomalacia (softening of bones) in adults and rickets in children. Combined calcium and vitamin D may reduce the risk of spinal fractures in patients with osteoporosis and, vitamin D plus calcium decrease the risk of hip fractures particularly among institutionalised persons. Vitamin D in combination with calcium may improve balance and muscle function, and reduce the risk of falls in elderly people.

VI.1.3. Unknowns relating to treatment benefits

It seems likely that vitamin D substitution improves muscle function and physical performance, particularly in elderly individuals, and among those with severe vitamin D deficiency. However, little is known if vitamin D substitution can provide additional benefits on physical performance among younger people or people with adequate vitamin D levels.

The active form of vitamin D (calcitriol) is known to regulate more than a hundred genes in many different tissues. Calcitriol is known to modulate the immune system. The
consequences of this in relation to autoimmune disease, cancer and cardiovascular function etc are not yet fully understood.

VI.1.4. Summary of safety concerns

<table>
<thead>
<tr>
<th>Important identified risks</th>
<th>What is known</th>
<th>Preventability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalcaemia (increased levels of calcium in the blood), hypercalciuria (increased levels of calcium in the urine).</td>
<td>Vitamin D increases the gastrointestinal uptake of calcium. Vitamin D should therefore be used with caution in patients with conditions known to have an increased risk of metabolism of vitamin D into its active form. Vitamin D should be used with caution in patients with impairment of renal function.</td>
<td>Follow the recommendation provided in the product information which states that Vitamin D₃ should not be used in patients with kidney problems or a history of kidney stones</td>
</tr>
<tr>
<td>Allergic (hypersensitive) reactions</td>
<td>The frequency of hypersensitivity reactions cannot be estimated.</td>
<td>Follow the recommendations given in the product information that colecalciferol should not be used by patients allergic to colecalciferol or any of the other ingredients of Divisun/Colecalciferol Meda.</td>
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<table>
<thead>
<tr>
<th>Important potential risks</th>
<th>What is known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D toxicity</td>
<td>Excessive dosing over long periods of time may constitute a risk. In man toxicity has not been reported at doses lower than 10,000 IU per day. With the maximum daily dosage 4000 IU there is a great safety margin to doses with a potential to cause toxicity.</td>
</tr>
<tr>
<td>Missing information</td>
<td>Use in children has not been studied. Use in patients with severe renal impairment has not been studied.</td>
</tr>
</tbody>
</table>

VI.1.5. Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these
documents are known as routine risk minimisation measures. The Summary of Product Characteristics and the Patient Information Leaflet can be found on the EPAR page. This medicine has no additional risk minimisation measures.

Not applicable. No additional risk minimisation measures are planned.

VI.1.6. Planned post authorisation development plan

No post authorization studies are planned.