PART VI: SUMMARY OF THE RISK MANAGEMENT

Summary of risk management plan for Strefen Direct 8.75 mg Oromucosal Spray (Flurbiprofen)

This is a summary of the risk management plan (RMP) for Strefen Direct 8.75 mg Oromucosal Spray. The RMP details important risks of Strefen Direct 8.75 mg Oromucosal Spray, how these risks can be minimised, and how more information will be obtained about Strefen Direct 8.75 mg Oromucosal Spray's risks and uncertainties (missing information) if applicable.

Strefen Direct 8.75 mg Oromucosal Spray's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Strefen Direct 8.75 mg Oromucosal Spray should be used.

I. The medicine and what it is used for

Strefen Direct 8.75 mg Oromucosal Spray is authorised for short term symptomatic treatment of sore throat in adults and adolescents over 12 years of age. It contains flurbiprofen as the active substance and it is given by oral administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Strefen Direct 8.75 mg Oromucosal Spray together with measures to minimise such risks and the proposed studies for learning more about Strefen Direct 8.75 mg Oromucosal Spray's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

II.A List of important risks and missing information

Important risks are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the product. Potential risks are concerns for which an association with the use of the medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Products marketed by RB have well-established safety profiles and can, therefore, be safely taken. The safety profile of Strefen Direct 8.75 mg Oromucosal Spray is positive; however, RB believes the risks below should be considered in this RMP for full oversight on all risks, but not to an extent that would warrant further investigations beyond its current risk minimisation measures. RB rigorously performs routine pharmacovigilance activities and regularly evaluates its safety information based on adverse event data, literature and advice from regulatory authorities. RB believes that the risks below are sufficiently mitigated through these routine measures.

Important Identified Risks	• Gastrointestinal disorders – particular among elderly patients, and those with a history of gastrointestinal disease, such as ulcerative colitis, Crohn's disease, bleeding, ulceration or perforation. • Renal disorders – particular among those patients with pre-existing renal insufficiency or prostaglandin-dependent conditions such as renal disease, dehydration, liver dysfunction, chronic heart failure and advanced age.
Important Potential Risks	• Potential for drug interactions – particularly with other NSAIDS; anti-platelet agents such as acetylsalicylic acid; anticoagulants such as warfarin. • Use of the drug during pregnancy – particularly for those women attempting to conceive, experience difficulty conceiving or undergoing fertility treatment, as well as women in their third trimester of pregnancy and breast-feeding women.
Missing Information	• None.

II.B Summary of important risks

Identified risks

Gastrointestinal disorders – particular among elderly patients, and those with a history of gastrointestinal disease, such as ulcerative colitis, Crohn's disease, bleeding, ulceration or perforation.	
Evidence for linking the risk to the medicine	Known safety profile due to well-established use, supported by literature, regulatory authorities and adverse event data.
Risk factors and risk groups	Patients with an active or history of a recurrent peptic ulcer/haemorrhage (2 or more distinct episodes of proven ulceration or bleeding), patients with a history of GI bleeding or perforation, and the elderly, who are at an increased risk of GI adverse reactions. The elderly, and any patient with a history of gastrointestinal disorders, are advised to comment treatment on the lowest effective dose and to report any unusual abdominal symptoms to their doctor or healthcare professional straight away.
Risk minimisation measures	Routine Risk Communication: Warnings within the SmPC: 4.3 Contraindications 4.4 Special warnings and precautions for use 4.5 Interaction with other medicinal products and other forms of interaction 4.8 Undesirable effects 4.9 Overdose Warnings within the PIL: 2. What you need to know before you use Strepfen Honey and Lemon 3. How to take Strepfen Honey and Lemon 4. Possible side effects
Additional pharmacovigilance activities	None

Renal disorders – particular among those patients with pre-existing renal insufficiency or prostaglandin-dependent conditions such as renal disease, dehydration, liver dysfunction, chronic heart failure and advanced age.	
Evidence for linking the risk to the medicine	Known safety profile due to well-established use, supported by literature, regulatory authorities and adverse event data.

Renal disorders – particular among those patients with pre-existing renal insufficiency or prostaglandin-dependent conditions such as renal disease, dehydration, liver dysfunction, chronic heart failure and advanced age.	
Risk factors and risk groups	Patients with pre-existing renal impairment
Risk minimisation measures	Routine risk communication: Warnings within the SmPC: 4.3 Contraindications 4.4 Special warnings and precautions for use 4.5 Interaction with other medicinal products and other forms of interaction 4.9 Overdose Warnings within the PIL: 2. What you need to know before you use Strepfen Honey and Lemon
Additional pharmacovigilance activities	None

Potential risks

Potential for drug interactions – particularly with other NSAIDS; anti-platelet agents such as acetylsalicylic acid; anticoagulants such as warfarin.	
Evidence for linking the risk to the medicine	Known safety profile due to well-established use, supported by literature, regulatory authorities and adverse event data.
Risk factors and risk groups	Patients undergoing concomitant therapy
Risk minimisation measures	Routine risk communication: Warnings within the SmPC: 4.4 Special warnings and precautions for use 4.5 Interaction with other medicinal products and other forms of interaction Warnings within the PIL: 2. What you need to know before you use Strepfen Honey and Lemon
Additional pharmacovigilance activities	None

Use of the drug during pregnancy – particularly for those women attempting to conceive, experience difficulty conceiving or undergoing fertility treatment, as well as women in their third trimester of pregnancy and breast-feeding women.	
Evidence for linking the risk to the medicine	Known safety profile due to well-established use, supported by literature, regulatory authorities and adverse event data.
Risk factors and risk groups	Pregnant or breastfeeding women
Risk minimisation measures	Routine risk communication: Warnings within the SmPC: 4.6 Fertility, pregnancy and lactation Warnings within the PIL: 2. What you need to know before you use Strepfen Honey and Lemon
Additional pharmacovigilance activities	None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Strefen Direct 8.75 mg Oromucosal Spray.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Strefen Direct 8.75 mg Oromucosal Spray as part of this decentralised procedure.