VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

The product is intended for general population, and the indication is for different oral mucosal conditions, including Oral Candidiasis , and gum diseases including gingivitis and periodontitis.

Oral Candidiasis is one of the most common oral mucosal conditions. Oral candidal colonisation has been reported to range from approximately 40% to 70% of healthy children and adults, with

higher rates observed among children with carious teeth and older adults wearing dentures. Candida carriage rate has been shown to also increase with cancer radiation therapy, diabetes, and HIV infection. Candida colonisation may lead to opportunistic mucosal infection as well as disseminated and multi-system organ involvement in immunocompromised people. The rate of infection has been reported as 50% during chemotherapy, 70% during radiation therapy, and 90% in HIV infection.[1]

Most cases of gingivitis are caused by plaque. Studies in Australia, Sweden, England, and Switzerland report gingivitis in 48-85% of children aged 3-6 years, but whether this range reflects population differences or whether it is due to different criteria used to define the disease is difficult to know. In adolescence, incidence around the world is comparable to US data (70-90[2]

Nearly half of American adults older than age 30 years have periodontal disease, the prevalence of periodontitis rises to 70.1% in adults older than age 65.[3]

VI.2.2 Summary of treatment benefits

The mouthwash that contains Chlorhexidine digluconate is used as Adjunct treatment in moth infections, post operative care following oral surgery. It's intended also as local antiseptic.

Chlorhexidine gluconate is used in 0.12% mouthwash for the prevention of plaque and the prevention and treatment of gingivitis and in the treatment of oral candidiasis, Gingivitis and periodontitis are two distinct chronic inflammatory processes belonging to the spectrum of periodontal diseases of the oral cavity affecting the tooth supporting tissues in response to bacterial accumulation.

This product has well established place in the therapy of this condition.

VI.2.3 Unknowns relating to treatment benefits

There are no relevant unknowns relating to treatment benefits.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Allergic reaction (Hypersensitivity)	Rare cases of hypersensitivity reactions have been reported	This effect is not preventable.

[1] Oral candidiasis. Epidemiology. Bestpractice 2013. Available at http://bestpractice.bmj.com/best-practice/monograph/106/basics/epidemiology.html. Accessed on 13-DEC-2013
[2] Stephen JM et al. Gingivitis. Epidemiology. Medscape 2013. Available at http://emedicine.medscape.com/article/763801-overview#a0199. Accessed on 13-DEC-2013
[3] Garcia J. Periodontitis Affects Nearly Half of Americans Over 30. Medscape Medical News 2013. Available at : http://www.medscape.com/viewarticle/772171. Accessed on 13-DEC-2013.

Risk	What is known	Preventability
	including severe allergic reactions with symptoms such as breathing problems, swelling around the eyes, low blood pressure, shock have also been reported after local application of chlorhexidine.	
Desquamative changes in the mucosa	Warning in case of ulcerations and erosive –desquamative exfoliation of the oral mucosa , the medicinal product should not be used	Should patients experience any Desquamative changes in the mucosa, medicinal product should be stopped.
Numbness of the tongue	Reversible numbness of the tongue.These symptoms generally improve over the course of use of medicinal product .	If the numbness of the tongue still persists after cessation of treatment, patient should consult a doctor or pharmacist.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Risk of bacterial and fungal spreading due to continuous use	Continuous use of the medicinal product could modify the oral microbial flora, this being associated with the risk of bacterial and fungal spreading (candidiasis). If symptoms persist after 5 days and/or are associated with fever, therapeutic options should be reconsidered

Missing information

Risk	What is known (Including reason why it is considered a potential risk)
Use in pregnancy and lactation	There is limited experience with the use of chlorhexidine in pregnant women. Also, it is not known, whether chlorhexidine is present in breast milk.

VI.2.5 Summary of 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 Package leaflet for PAROEX 1.2 mg/ml, mouthwash can be found in the competent authority's webpage.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post authorisation development plan was proposed by the Applicant.

VI.2.7 Summary of changes to the Risk Management Plan over time

Table 2. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
02.00	06-JAN-2015	Important identified risk: Hypersentivity Important potential risk: None identified Missing information: Use in pregnancy and lactation	Initial version.
03.00	30-June-2015	**Important identified risk**: • Hypersentivity • Desquamative changes in the mucosa • Numbness of the tongue **Important potential risk**: • Risk of bacterial and fungal spreading due to continuous use **Missing information**: • Use in pregnancy and lactation	Important identified and potential risks have been added as per assessor's comments.
04.00	25-August 2015	**Criteria for judging the success of the proposed risk minimisation measures** <u>Important identified risk</u> Hypersensitivity: ≤ 3 cases/year Desquamative changes of the mucosa: ≤ 2 cases/year Numbness of the tongue: ≤ 2 cases/year <u>Important potential risk</u> Risk of bacterial and fungal spreading due to continuous use: ≤ 1 cases/year <u>Missing information</u> Use in pregnancy and lactation: limited use of the product in this population: < 5.0% of adverse events are reported in pregnant or breast-feeding women	The criteria for the assessment of safety data for each safety concern is specified as per Bfarm assessor's comments.

Version	Date	Safety Concerns	Comment
05.00	12-January 2016	1) The effectiveness of the risk minimisation measures is presented for each safety concern separately (no summary in one table 2) The section "Planned dates for assessment" is revised as follows **Planned dates for assessment** ~~Annually after authorisation of the product~~ *Continuously - in accordance with signal detection requirements (IX.C.1.5 Roles and responsibilities of marketing authorisation holders -GVP Module IX).* **Results of effectiveness measurement** Not applicable, this is the initial version of this RMP. **Impact of risk minimisation** Broad impact is expected in the target population. **Comment** N/A	Revision as per Bfarm assessor's comments in the D210 FAR