VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

HIV infection

HIV stands for human immunodeficiency virus. It kills or damages the body's immune system cells. AIDS stands for acquired immunodeficiency syndrome. It is the most advanced stage of infection with HIV. HIV most often spreads through unprotected sex with an infected person. It may also spread by sharing drug needles or through contact with the blood of an infected person. Women can give it to their babies during pregnancy or childbirth. Globally, an estimated 35.3 million people were living with HIV in 2012 and 2.3 million new HIV infections globally. At the same time the number of AIDS deaths is also declining with 1.6 million AIDS deaths in 2012, down from 2.3 million in 2005. In June 2014, a total of 17,750 persons (17,558 adults and 192 children and adolescents) living with HIV in the Netherlands with low death rates. In western and central Europe, estimated occurrence of HIV infection were noted in range of 770,000 - 930,000 people.

VI.2.2 Summary of treatment benefits

Nevirapine, taken in combination with two other antiviral medicines, was more effective than combinations of two medicines. In 398 treatment-experienced adults (who had taken treatment for HIV infection before), Nevirapine in combination with zidovudine and lamivudine led to a 38% reduction in viral load after 48 weeks, compared with a 28% rise in those taking zidovudine and lamivudine without Nevirapine. In 151 treatment-experienced patients (who had not taken treatment for HIV infection before), viral load fell by 99% in the three-medicine group, compared with 96% in the two-medicine group after 40 to 52 weeks. Adults taking three medicines also had greater rises in blood cell (CD4 cell) counts, and a lower risk of their disease getting worse or of dying. Similar results were seen in HIV-1-infected children.

VI.2.3 Unknowns relating to treatment benefits

Data on safety and efficacy of nevirapine in Children aged less than 3 years, patients over the age of 65 and patients with renal dysfunction has not been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Severe Skin reactions (Skin rash, including severe or life-threatening skin reactions, e.g. Stevens-Johnson syndrome and toxic epidermal necrolysis)	The most important side effects of nevirapine is severe and life threatening skin reactions. These reactions occur mainly in the first 18 weeks of treatment with nevirapine. This is therefore an important period which requires close monitoring by your doctor. When rash occurs it is normally mild to moderate. However, in some patients a rash, which appears as a blistering skin reaction, can be severe or life-threatening (Stevens-Johnson syndrome and toxic epidermal necrolysis) and deaths have been recorded. Most of the cases of both severe rash and mild/moderate rash occur in the first six weeks of treatment. If rash occurs and you also feel sick, you must stop treatment and visit	During the first 18 weeks of treatment with nevirapine it is very important that you and your doctor watch out for signs of skin reactions. These can become severe and even life threatening. You are at greatest risk of such a reaction during the first 6 weeks of treatment. You should discontinue taking nevirapine and you must contact your doctor immediately as such reactions can be potentially life-threatening or lead to death. If you develop severe skin reactions whilst taking nevirapine, NEVER TAKE NEVIRAPINE again without referring to your doctor.

	your doctor immediately.	
Severe liver reaction (Severe and life-threatening hepatotoxicity, including fatal fulminant hepatitis)	The most important side effects of nevirapine is severe and life threatening liver reaction. Abnormal liver functioning has been reported with the use of nevirapine. This includes some cases of inflammation of the liver (hepatitis), which can be sudden and intense (fulminant hepatitis), and liver failure, which can be both fatal.	During the first 18 weeks of treatment with nevirapine it is very important that you and your doctor watch out for signs of liver reactions. These can become severe and even life threatening. You are at greatest risk of such a reaction during the first 6 weeks of treatment. If you experience symptoms suggesting damage of the liver, such as loss of appetite, feeling sick (nausea), vomiting, yellow skin (jaundice), abdominal pain; you should discontinue taking nevirapine and must contact your doctor immediately. Do not take nevirapine if you have severe liver disease or if you have had to stop nevirapine treatment in the past because of changes in your liver function.
A reduction in the numbers of white blood cells, particularly in children which increasing the risk	A reduction in white blood cells (granulocytopenia) can occur, which is more common in children. As with rash symptoms, please inform your doctor of any side effects.	If you get any side effects, talk to your doctor or pharmacist.

of infection (Granulocytopenia, particularly in paediatric population)		

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.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

No studies planned.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety Concern	Comment
2.0		**Part II – Module SVIII** Below safety concerns have been removed from the RMP: **<u>Important identified risks</u>** • Osteonecrosis	As per RMS Day 70 preliminary assessment report for Nevirapine XR Hetero (NL/H/3536/001/DC) dated 08 October 2015, the RMP has been updated.

Version	Date	Safety Concern	Comment
		• Immune Reactivation Syndrome • Interaction with products metabolised by CYP3A4 and CYP2B6 and interaction with CYP3A4 inhibitors **Important potential risks** • Use in pregnancy	