Summary of risk management plan for imatinib

This is a summary of the risk management plan (RMP) for imatinib. The RMP details important risks of imatinib and how more information will be obtained about imatinib's risks and uncertainties (missing information).
Imatinib's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how imatinib should be used.
Important new concerns or changes to the current ones will be included in updates of imatinib's RMP.

I. The medicine and what it is used for

Imatinib is authorised for treatment of several types of neoplastic diseases in both adult and paediatric populations, primarily haematological neoplastic diseases (chronic myeloid leukaemia, acute lymphoblastic leukaemia, myelodysplastic/myeloproliferative diseases, advanced hypereosinophilic syndrome) as well as gastrointestinal stromal tumours (GIST) and dermatofibrosarcoma protuberans (DFSP) (see SmPC for the full indication). It contains imatinib as the active substance and it is taken orally.

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

Important risks of imatinib, together with measures to minimise such risks and the proposed studies for learning more about imatinib'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.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of imatinib is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of imatinib are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of imatinib. Potential risks are concerns for which an association with the use of this 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);

List of important risks and missing information	
Important identified risks:	None
Important potential risks:	Second primary malignancy
	Tolerability during pregnancy and pregnancy outcomes
Missing information:	Pediatric patients: long term follow up
	Pediatric patients below 2 years of age

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 imatinib.

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

There are no studies required for imatinib.

Annex 4 - Specific adverse drug reaction follow-up forms

Follow-up questionnaires for spontaneous adverse event reports of:

Safety during pregnancy

- **Pregnancy report form**
- **Pregnancy outcome form**

TARGETED REPORT FORM / FOLLOW-UP QUESTIONNAIRE

(SAFETY DURING PREGNANCY)

Pregnancy report form

Maternal data					
Country	**Initials**	**Date of birth (DD/MM/YYYY) Age**	**Ethnicity**	**Weight (kg)**	**Height (cm)**
	(first, last)				
Last Menstrual Period (DD/MM/YYYY)	**Expected Date of Delivery (DD/MM/YYY)**	**Occupation**	**Education Level**		

Mother's medical history and risk factors

Has the patient any relevant medical history or risk factors? Please indicate as appropriate.

				If YES, please specify (including onset date):
Endocrinological problems	**UNK** ☐	**NO**☐	**YES**☐	
Recent infections or diseases which needed treatment	**UNK** ☐	**NO**☐	**YES**☐	
Fertility problems or use of fertility methods	**UNK** ☐	**NO**☐	**YES**☐	
Recreational drugs	**UNK** ☐	**NO**☐	**YES**☐	
Chemical exposure	**UNK** ☐	**NO**☐	**YES**☐	
X-rays	**UNK** ☐	**NO**☐	**YES**☐	

Decreased pregnancy rate	**UNK** ☐	**NO**☐	**YES**☐
Family history of malformation, significant obstetric outcome or heredity disorders	**UNK** ☐	**NO**☐	**YES**☐
Drug or alcohol abuse	**UNK** ☐	**NO**☐	**YES**☐
Smoking	**UNK** ☐	**NO**☐	**YES**☐
Other	**UNK** ☐	**NO**☐	**YES**☐

Contraception used prior to pregnancy

Please specify:

Pregnancy due to

Please indicate as appropriate.

☐ **Unsuccessful at abstinence**	☐ **Used ineffective contraception**	☐ **Unexpected sexual activity**
☐ **Contraceptive failure**	☐ **Planned**	☐ **Other (please specify):** _____

Previous pregnancies

Please provide the number for each pregnancy category:

Gravida (# of times pregnant)	
Para (# of successful deliveries > 20 weeks gestation)	
Abortus (#of fetal losses < 20 weeks gestation)	

Please describe any abnormal outcomes (include elective abortions, miscarriages, and malformations) including dates if known:

Date	**Outcome**

In case of a previous abnormal pregnancy outcome, list all known medications used:

Drug name	**Route**	**Dosing regimen**	**Indication for use**	**Therapy dates (start-end)**

Current condition

Please list any chronic and/or ongoing medical conditions that started prior to pregnancy.

_____

_____

_____

Please list any acute medical conditions that have occurred since pregnancy began, and trimester during which the illness occurred.

_____

_____

_____

When was current condition confirmed: _____ (date)

Current condition (please indicate)

☐ Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML)

☐ Ph+ CML in chronic phase

☐ Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL)

☐ myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements

☐ advanced hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukaemia (CEL) with FIP1L1-PDGFRα rearrangement

☐ Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST)

☐ risk of relapse following resection of Kit (CD117)-positive GIST

☐ unresectable dermatofibrosarcoma protuberans (DFSP) or recurrent and/or metastatic DFSP

Was patient hospitalized: _____(date)

How long was patient hospitalized: _____(date)

Did patient received any other treatment?

☐ **yes**

☐ **no**

What kind of treatment did the patient receive?

☐ **bone marrow transplantation**

☐ **interferon-alpha therapy**

☐ **chemotherapy**

☐ **surgical treatment**

☐ **none**

Present pregnancy

Please complete the following:

Exposure via	☐ **Maternal Exposure**
Product Route	
Dose	
Start Date	
Stop Date	
Indication	
Lot Number	
What other medications has the mother used since last menses date? (Include Rx, OTC, and vitamins?	
Medication Indication	
Start Date (DD/MM/YYYY)	
End Date/ Ongoing (DD/MM/YYYY)	

Was a prenatal test done?

UNK☐ **NO**☐ **YES**☐

If YES, please complete below.

Test	**Date**	**Evidence of defect?**	**If YES, please describe defect**
Ultrasound		**U N Y** **N O E** **K** ☐ **S** ☐ ☐	

Amniocentesis			
MSAFP/serum markers			
Other: (e.g. Chorionic Villi sampling, serology tests)			

What is the status of the current pregnancy? Please select as appropriate.

☐ **Continuing** ☐ **Missed abortion**

☐ **Spontaneous abortion** ☐ **Ectopic pregnancy**

☐ **Elective abortion** ☐ **Unknown False positive pregnancy test**

☐ **Threatened abortion** **If ABORTION, date of abortion:**

TARGETED REPORT FORM / FOLLOW-UP QUESTIONNAIRE

(SAFETY DURING PREGNANCY)

Pregnancy outcome form

Maternal data					
Country	**Initials**	**Date of birth (DD/MM/YYYY) Age**	**Ethnicity**	**Weight (kg)**	**Height (cm)**
	(first, last)				
Last Menstrual Period (DD/MM/YYYY)	**Expected Date of Delivery (DD/MM/YYY)**	**Occupation**	**Education Level**		

Course and Outcome of Pregnancy

Did the mother experience any medical problems during this pregnancy?

NO□ **YES□**

If YES, please complete below.

Event	**Trimester of occurrence**

Did the mother take any medications during this pregnancy? (include Rx, OTC and vitamins, but exclude medications used during labour and delivery)

NO□ **YES□**

If YES, please complete below.

Product exposure via: Male Partner/	**Medication**	**Indication**	**Trimester of occurrence**

Maternal Exposure			

Did the mother receive any medication during labour and delivery? (include anaesthesia)

NO☐ **YES☐**

If YES, please complete below.

Medication	Start date	End date / Ongoing	Indication

Specify the outcome of pregnancy and complete the rest of the form as applicable (tick as applicable)

☐ **Spontaneous abortion** **Date:** _____

☐ **Induced abortion** **Date:** _____

☐ **Uninterrupted pregnancy** **Delivery Date:** **Gestational age:**

Delivery Method

☐ **Spontaneous**

☐ **Forceps**

☐ **Vacuum extract**

☐ **Caesarean section**

☐ **Induced**

☐ **Other: please specify: _____**

Were there any labour/delivery complications (e.g. fetal distress, amniotic fluid abnormal, abnormal placenta)

NO☐ **YES☐**

Please describe:

Characteristics of the Baby

General Appearance:

Sex	**Male**☐ **Female**☐
Apgar score: 1 min, 5 min, 10 min	
Term/ Preterm/ Post term	
Weight	
Length	
Head circumference	

Clinical condition of the baby:

☐	**Healthy Baby**		
☐	**Prematurity**		**Specify gestational age:**
☐	**Congenital abnormality**	**Specify:**	**Possible Cause:**
☐	**Neonatal problem**	**Specify:**	**Possible Cause:**
☐	**Neonatal death***	**Date:**	**Possible Cause:**
☐	**Stillbirth***	**Date:**	**Possible Cause:**

***Was a foetal autopsy done?**

NO☐ **YES**☐

Please describe: (attach copy of report if available)

Follow-up Examination of the Baby:

Date	**Findings**

Relevant laboratory Tests / Procedures for Baby / Fetus

Was there any laboratory tests / procedures done for the baby / fetus?

NO☐ **YES**☐

If YES, please complete below.

Test / Procedure	Date	Result

Additional information

Was the baby's hospitalization prolonged?

NO☐ **YES**☐

If YES, please describe:

Did the baby receive any special treatment?

NO☐ **YES**☐

If YES, please describe:

Was any relationship suspected between the abnormal pregnancy outcome and exposure to the product?

UNK☐ **NO**☐ **YES**☐

If YES, please describe:

Are there any other factors that may have contributed to this outcome?

NO☐ **YES**☐

If YES, please describe:

Was there any relationship between the abnormal pregnancy outcome and the use of concomitant medications?

NO☐ **YES**☐

If YES, please describe: