6.2. Elements for a Public Summary

6.2.1. Overview of Disease Epidemiology

Chronic pain is pain that is ongoing and recurring for lengthy periods of time.² Globally, 1 out of 10 adults are diagnosed with chronic pain each year.³ The estimated prevalence of chronic pain in Europe ranges from 19% to 31% and in the US it is 33% to 64%.^{4,5,6,7} Chronic pain generally increases with age and has been diagnosed more commonly in women than in men.^{8,9} The negative impact of chronic pain includes depression, inability to work, disrupted social relationships, and suicidal thoughts.³ Five common conditions underlying chronic pain are cancer pain, neuropathic pain, osteoarthritis pain, rheumatoid arthritis pain, and chronic low back pain. Medical conditions associated with chronic pain include depression, anxiety, and sleep disturbance.

6.2.2. Summary of Treatment Benefits

Fentanyl transdermal patch is used for treatment of severe and long-lasting pain that can only adequately be managed with strong pain relievers (opioids) in adults and in children 2 years or older. It can provide relief to adults and children over 2 years old who need round-the-clock control of severe, long-lasting pain. The patch releases medicine slowly and steadily for up to 3 days.

Fentanyl citrate solution for injection is used in adults and in children 2 years or older who are already using strong pain medication but who need additional pain control from time to time. It can also be given before or during surgery for pain control.

6.2.3. Unknowns Relating to Treatment Benefits

Other than Missing Information (pediatric patients less than 2 years old and pregnancy and lactation), there are no unknowns relating to treatment benefits of which the MAH is aware.

Fentanyl was originally developed and investigated by another company, so Pfizer cannot fully comment on whether those clinical trials fully covered every type of patient who might be prescribed fentanyl.

6.2.4. Summary of Safety Concerns

6.2.4.1. Important Identified Risks

Risk	What is Known	Preventability	
Breathing more slowly	Fentanyl can dangerously suppress breathing in	Patients who breathe more	
or weakly (respiratory	any patient, leading to low body oxygen,	slowly or weakly while using	
depression)	unconsciousness, and even death. The risk of side	fentanyl should discontinue	
1 /	effects is higher in patients with lung problems or	treatment and immediately	
	breathing problems. Sometimes a lower dose of	contact a doctor or visit a	
	fentanyl is prescribed in these situations.	hospital.	
Drug dependence and	Physical or psychological dependence and	Patients who have been	
withdrawal	symptoms of withdrawal may develop for repeat	dependent or shown	
	use of opium-like substances (opioids).	withdrawal while taking	
		alcohol, prescription	
		medicines, or illegal drugs	
		should be monitored for signs	
		of dependence or withdrawal.	
Abuse, misuse, and	Resistance (tolerance) may develop for repeat use	Patients who have ever abused	
diversion	of opium-like substances (opioids). Abuse or	or been dependent on alcohol,	
41 (415.511	intentional misuse of fentanyl may result in	prescription medicines, or	
	overdose and/or death.	illegal drugs should be	
	overtices und or usual.	monitored for signs of misuse,	
		abuse, or addiction.	
Accidental exposure	Accidental exposure to fentanyl patches has	Patients should dispose of used	
Tree and the posterior	occurred, mainly because of confusion over	and unused patches properly.	
	product packaging, accidental transfer and	Used patches should be folded	
	improper disposal of the used product. To	inward so that the sticky sides	
	minimise the risk of accidental exposure to	meet. Unused patches should	
	fentanyl patches, the name and strength of the drug	be returned to the hospital or	
	on the patch are now printed in long-lasting ink	pharmacy.	
	that can be seen clearly by patients and caregivers.	production of the production o	
	This change should help patients and caregivers		
	find patches on patients' bodies and see patches		
	that have fallen off, which children and pets could		
	accidentally touch or eat. In addition, the SmPC		
	and Patient Leaflet have been revised to include		
	warnings concerning this risk. Section 4.4		
	(Special warnings and precautions for use) and		
	Section 6.6 (Special Precautions for Disposal) of		
	the core patch SmPC and corresponding changes		
	to the Patient Leaflet have all been amended to		
	warn patients and caregivers concerning potential		
	accidental transfer of patches and the importance		
	of proper disposal of used patches.		
Medication error	Medication errors can result from mistakes by	Use these patches only as	
	physicians, pharmacists, patients or caregivers. In	instructed by your health care	
	order to avoid medication errors, the SmPCs and	provider. The outer packaging	
	package leaflets should be read carefully before	of each patch should be	
	this medicine is used and kept for future reference.	consulted to verify the dose of	
	Any questions should be referred to the	the patch before it is applied to	
	prescribing physician or the pharmacist. If the	the skin.	
	patient experiences any side effects, contact the		
	patient's doctor or pharmacist.		
Overdose	Overdose can result from prescribing errors by	Patients should use these	
	physicians, dispensing errors by pharmacists,	patches only as instructed by	

Risk	What is Known	Preventability
	administration errors by patients or their	their health care provider.
	caregivers, suicide attempt, and abuse (including	When replacing patches,
	tampering with the product). The risk of overdose	remove used patch(es) first
	is minimised by the SmPCs and package leaflets.	before applying next patch(es)
	The SmPCs and package leaflets give information	to skin.
	about taking or using a medicine. In order to	
	avoid medication errors, the SmPCs and package	
	leaflets should be read carefully before this	
	medicine is used. The SmPCs and package	
	leaflets should be kept for future reference if	
	needed and any questions should be referred to the	
	prescribing physician or the pharmacist who	
	dispensed this product. If the patient experiences	
	any side effects, the patient's doctor or pharmacist	
	should be contacted. The patient should not	
	tamper with the patch.	

SmPC = Summary of Product Characteristics.

6.2.4.2. Important Potential Risks

Risk	What is Known (Including Reason Why it is Considered a Potential Risk)
Serotonin syndrome	Serotonin syndrome can result from use of fentanyl with drugs that affect the
	nervous system, including certain medicines used to treat depression and other
	psychiatric conditions. If the patient experiences any side effects consistent
	with serotonin syndrome (e.g., mental-status changes, autonomic instability,
	neuromuscular abnormalities or gastrointestinal symptoms), the patient's
	doctor or pharmacist should be contacted.

6.2.4.3. Missing Information

Risk	What is Known
Safety and efficacy in children <2 years of age	Not enough information is available on the use of fentanyl in children less than 2 years old. Fentanyl should not be used in children less than 2 years
<2 years or age	old.
Safety and efficacy of use during pregnancy and lactation	Not enough information is available on the use of fentanyl in pregnant women. Animal reproduction studies with fentanyl have shown reproductive harm. The potential risk for humans is unknown. Fentanyl should not be used during pregnancy unless necessary. Fentanyl should not be used during childbirth because it may cause the newborn infant to breathe more slowly or weakly. Fentanyl is excreted into human milk. Fentanyl should not be used by breastfeeding women.

6.2.5. Summary of Additional Risk Minimisation Measures by Safety Concern

The Summary of Product Characteristics (SmPC) for fentanyl provides physicians, pharmacists, and other health care professionals with details on how to use the medicine, the risks, and recommendations for minimising risks. An abbreviated version of this in lay language is provided in the form of the package leaflet. The measures in these documents are known as routine risk minimisation measures. The SmPC and the package leaflet for fentanyl are in the applicant's European Public Assessment Report (EPAR) page.

This medicine has no additional risk minimisation measures.

6.2.6. Planned Post-Authorisation Development Plan

No post-authorisation studies are planned.

6.2.7. Studies that are a Condition of the Marketing Authorisation

None.

6.2.8. Summary of Changes to the Risk Management Plan Over Time

Table 6. Major Changes to the Risk Management Plan Over Time

Version	Date	Safety Concerns	Comment
1.0	Submitted on 20 October 2013	Important identified risks: • Abuse/intentional misuse/addiction/ dependence • Respiratory depression • Hypotensive effects • Drug/drug interactions Important potential risk: • Medication errors Important missing information: • Pediatric patients less than 2 years old • Pregnancy and lactation	Initial RMP
1.1	22 April 2014	Important identified risks: Respiratory depression Drug dependence and withdrawal Abuse, misuse, and diversion Important potential risks: Accidental exposure Medication error Overdose Serotonin syndrome Important missing information: Safety and efficacy in children <2 years of age Safety and efficacy of use during pregnancy and lactation	Updated in response to preliminary variation assessment report for Type II Mutual Recognition Procedure variation DE/H/2556/001-005/II/009
1.2	04 August 2014	Important identified risks	Updated in response to Type II final variation assessment report DE 2556 II 009 FVAR