SFETD

Société Française d'Étude et de Traitement de la Douleur

ITAT

Intrathecal Analgesia Toolbox

EDITORIAL

Intrathecal analgesia is a highly effective technique for relieving intractable pain, particularly in oncology. This invasive technique has demonstrated its usefulness when strong opioid treatments fail or when their adverse side effects are a problem.

Unfortunately, in France today, the potential of intrathecal analgesia to treat pain is still underexploited. Healthcare professionals are insufficiently informed about intrathecal analgesia and do not use it often enough. It can be daunting as its implementation requires planned organization and expertise.

Today, the SFETD is proud to present the *Intrathecal Analgesia Toolbox*, an educational handbook featuring numerous illustrations, tables and all the practical information you need to set up this analgesia.

This handbook is the work of a large panel of experts in the field, whose single purpose is to make this technique accessible to as many patients as possible.

Valeria Martinez

President, SFETD

PREFACE INTRATHECAL TOOLBOX

Over the past decade, intrathecal analgesia has become an essential addition to our armory of means to relieve refractory pain, particularly in oncology. This innovative technique gives relief to patients for whom there were previously few or no effective therapeutic options. Over the past thirty years, its use has expanded in all developed countries. In France, only in March 2009 was it fully recognized for insurance purposes by the national social security system, which now covers the medical devices, hospitalization for implantation, and repeated pump filling. However, this lost time has since been amply made up, and the technique is now more and more widely used. Meanwhile, the technique has earned official healthcare recognition in France, first by the Formalized Expert Recommendations of the SFETD and SFAR in 2013, then by the DGOS Instruction in 2017 and finally by the HAS Recommendations in 2020. The active support of other learned societies such as AFSOS, SFAP and the Société Française de Neuromodulation, and of the INCA, must also be highlighted. Finally, the work of the SFETD's ambulatory care commission has ensured that hospital stays for pump refilling are adequately covered by insurance.

These achievements belong first and foremost to all the physicians and other healthcare professionals who have invested in this new therapeutic option. We emphasize the key role played by the pain and cancer group set up within the SFETD, and in particular that of Dr Florence Tiberghien, who not only created the Toolbox, but also coordinated the efforts deployed in producing this handbook. We applaud the two years of commitment and the unstinting work of the whole group and of the authors of this indispensable documentary resource.

This handbook provides essential, precise practical information on the management of patients receiving intrathecal analgesia. Information begins with the prior requirements for implementing the therapy. This includes the essential step of collegial decision-making for implementation, with the help of the RCP (multidisciplinary meeting). This is now easier to organize using videoconferencing tools. The essential involvement of the hospital pharmacy in the implementation process is also clearly presented. Patient selection criteria and constraints are described in detail, particularly for cancer patients. The peri-operative period is also described in detail. The handbook provides both precise answers to the questions that will inevitably arise during the titration period, and invaluable aid for the management of complications. Administrative management is fully addressed at every stage of the procedure, together with the data required for costing the technique.

It goes on to provide detailed assistance in organizing and carrying out refilling and programming, and in diagnosis and management of complications. Illustrations and decision trees at each stage ensure easy access to information.

We are greatly indebted to the authors of this impressive handbook. I am convinced it will become a reference for all those in charge of patients receiving intrathecal analgesia and will impel further development of this new and important technique.

Denis Dupoiron

1 A TOOLBOX FOR INTRATHECAL ANALGESIC THERAPY IN THE RELIEF OF CANCER PAIN: WHY?

At the initiative of French practitioners and under the aegis of the SFETD, this handbook has been designed as a toolbox for pain teams wishing to develop intrathecal analgesia. The authors have no conflicts of interest relevant to this handbook. Images are made available to the SFETD free of charge by Medtronic.

Some 15% [1] of cancer patients with pain have refractory or intractable pain, particularly in the advanced stages of the disease. Intrathecal analgesia should be made available in all of France to ensure equal access to care. This objective is still far from being achieved.

This handbook gives information on day-to-day practice, whether your care entity is an implant facility and/or a conventional hospitalization facility for initiating intrathecal treatment, and/or a downstream facility providing follow-up and refilling, or a care department receiving a patient undergoing intrathecal analgesic treatment.

The situations described in what follows are meant to be suitably adapted to your local resources and are a practical aid only.

This handbook comprises practical information worksheets in five main sections, arranged chronologically to follow the patient's care pathway when applying this intrathecal analgesia technique:

- **Pre-implantation phase** with five worksheets
- **Implantation phase** with four worksheets
- **Post-implantation phase** with four worksheets
- **Possible complications** with two worksheets
- **11 practical worksheets**

If you want to learn more about intrathecal analgesic therapy, and if you would like to develop it in your care institution but have been hesitant, then now is the time to read this handbook.

Members of the Intrathecal Analgesia Toolbox working group of the SFETD Pain and Cancer Commission:

Olivier Giet Colmar, Anne Balossier Marseille, Denis Baylot Lyon, Christine Villatte Clermont-Ferrand, Denis Dupoiron Angers, Florence Tiberghien Haute-Savoie, Brigitte George Paris, Homauon Alipour Saint-Brieuc, Sabrina Jubier-Hamon Angers, Julie Berard IDE Paris, Rita Kortbaoui-Saad Paris, Olivier Renard Lyon ,Yves-Marie Pluchon La Roche-sur-Yon, Romain Chiquet Lille, Sylvie Rostaing Avignon, Jeremy Sorrieul Angers Pharmacist, Julien Robert Angers Pharmacist, Bich Dang Vu Paris

For translation and review: Richard Bryan and Virginie Guastella

[1] Meuser T, Pietruck C, Radbruch L, Stute P, Lehmann KA, Grond S. Symptoms during cancer pain treatment following WHO-guidelines: A longitudinal follow-up study of symptom prevalence, severity and etiology. Pain. 2001 Sep;93(3):247-257. doi: 10.1016/S0304-3959(01)00324-4. PMID: 11514084.

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I.1 PRIOR REQUIREMENTS FOR STARTING THERAPY

Key message: "Be ready and able to offer this technique to patients and ensure their follow-up in complete safety."

IDENTIFYING NEEDS :

It is important:

- To know whether intrathecal analgesia is already performed locally and whether the need for this technique is already met region-wide so that it can be offered to all patients,
- To differentiate levels of involvement: implant center and treatment initiation, center providing follow-up and refills, or both, as needs will be different.
- **Identify staff motivated** to create and train a team dedicated to intrathecal analgesia and able to provide ongoing care:
- Implanting anesthetist or neurosurgeon (see Worksheet II.2),
- Follow-up and refill physicians:
  - Motivated volunteer physicians,
  - Physicians already trained or in training, or who can be trained: at least two physicians already operational to start with,
- Coordination (nurse and secretary),
- Nurses trained in the technique or amenable to training: at least two nurses.
- **Mandatory partnership with the in-house pharmacy** of the care facility, irrespective of whether or not it makes up and issues treatment syringes itself:
  - Summary presentation of project and requirements: for feasibility analysis in terms of organization (patient circuit, drug circuit Worksheet I.2) and safety (to ensure compliance),
  - Agreement in principle on the preparation or dispensing of intrathecal drug solutions,
  - Necessary equipment: laminar flow hood (specific to intrathecal analgesia) if preparation is required,
  - Dedicated staff (pharmacist, assistants) with availability,
  - Drugs required:
    - Agents at desired concentrations,
    - Availability of ziconotide in the compounding pharmacy.

INVENTORIES OF PREMISES

- Technical platform for implant centers,
- To equilibrate the patient after surgical implantation: full hospitalization bed,
- For pump filling and programming (intrathecal therapy monitoring),
- Home care for teams who can refill pumps at home (e.g., terminally ill patients or those with complex travel arrangements).

ADMINISTRATIVE PROCEDURES: TO BE ADAPTED TO EACH CARE FACILITY

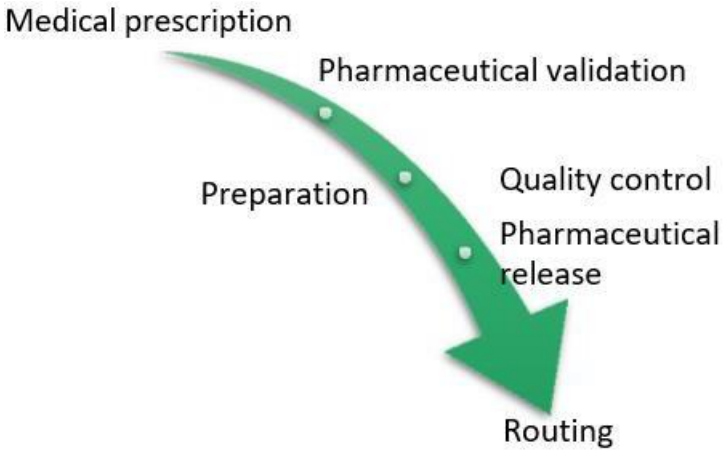
- Draw up a service project as part of overall organizational planning validated by the relevant authorities,
- Organize the collaboration of all the entities concerned,
- A telephone hotline should be planned. Feasibility, remuneration, organization specific to each care entity.

- **Partnerships and collaborations:** information and awareness raising of our partners concerning the benefits of the technique, the patient's care pathway, indications, etc.
    - Implant physicians
    - Chronic pain care structure
    - Radiation oncologists
    - Mobile Palliative Care Team, Palliative Care Units
    - Home care
    - Interventional radiologist
    - General medical practitioners
    - **Equipment manufacturers: essential partners for getting started**
        - Only one pain drug infusion pump is currently marketed: SynchroMed® II from Medtronic.
        - Find out about the available equipment and how it works: intrathecal catheters (externalized or implantable), programmable implantable pumps, external pumps, etc.
        - Provide documentation for healthcare professionals: pump types, filling kits, patient logbooks, binders, etc. Technical assistance , etc.
        - Plan documentation for patients (pumps, remote control, etc.)
        - Technical assistance for start-up.
- **Need for an IT tool to secure intrathecal prescribing** (free choice)
    - Excel software
    - Other software (Alma),
    - Other prescription software compatible with the in-house computerized information system (in collaboration with the IT department).

"Have staff available for mentoring during the implementation of the technique and afterwards if necessary."

I.2 PHARMACY CIRCUIT

The role of the pharmacist is essential in ensuring the safe preparation of the analgesic mixture, in accordance with local regulations.



Routing: warning of narcotic drug

Carrier authorized to transport drugs

Container stating the transport of narcotic drugs

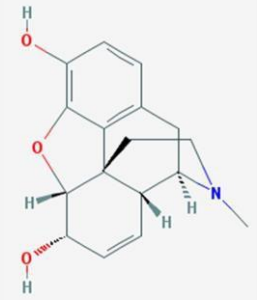
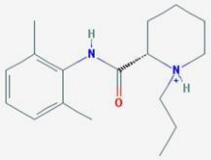
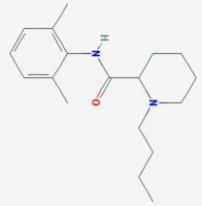
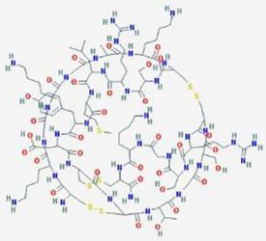
DRUG PREPARATION

- You need a qualified (inspected) ISO 5 cleanroom available on a regular basis, and hood-type equipment (microbiological safety station).
- Use of narcotics: one prescription, one preparation. One preparation, one named patient.
- Mandatory traceability of raw materials used: dosage forms, assays, batch expiry dates.
- Traceability to prescriber for narcotics (morphine, sufentanil, fentanyl).
- Planned traceability through to administration.

STORAGE

- Ideally, the syringe should be kept refrigerated in the dark to prevent plasticizer release from the syringe (between +2 and +8°C).
- Stability depends on the mixture (see Worksheet I.3). For example, a mixture of morphine/ropivacaine and ziconotide is stable for 3 days in syringes. A morphine-only mixture, on the other hand, is stable for longer.

I.3 INTRATHECAL DRUG TREATMENTS

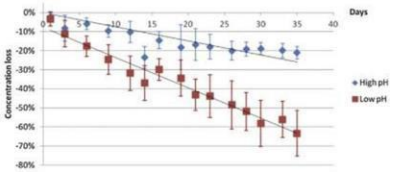
Drug	**Morphine**	**Ropivacaine**	**Bupivacaine**	**Ziconotide**
Classification and chemical structure	Opioid analgesic 	Long-acting local analgesic 		Other analgesic 
Target and mechanism of action	Competitive agonist of **opiate receptors**, primarily Mu, secondarily Kappa ○ Inhibition of adenylate cyclase ➡ Diminution of AMPc ○ Activation of potassium channels ○ Inactivation of calcium channels ➡ Hyperpolarization **End result** ○ Diminution of nerve conduction and reduced release of nociceptive neurotransmitters ○ Blockage of perception of pain signals	Reversible decrease in nerve fiber membrane permeability to **sodium ions** ○ Decreased depolarization rate ○ Increased excitation threshold **End result** Local blockade of nerve impulses	Stabilization of neuron membranes ○ Prevents production and transmission of nerve impulses **End result** Local blockade of nerve impulses	Direct inhibition of **voltage-dependent calcium channels** in primary nociceptive afferent nerve endings ⬇ Inhibition of nociceptive neurotransmitter release (including substance P) **End result** Blockade of perception of pain signals
Indications	Intense pain, especially nociceptive	Intense neuropathic pain	➡ Intense neuropathic pain	Intense chronic pain in adults **Intrathecal route only**

Drug	**Morphine**	**Ropivacaine**	**Bupivacaine**	**Ziconotide**	
Recommended initial dose	1/100 dose IV/day = 1/300 dose oral/day Do not exceed 5 mg/24 h	6–8 mg/day Initial dosage according to level of catheter	0.01 to 4 mg/day	0.25–0.50 µg/day Initial dosage according to level of catheter	
Main adverse effects	Nausea, vomiting, constipation, respiratory depression, cardiovascular depression, sedation or sometimes excitation, confusion, intracranial hypertension	Paresthesia/ hypoesthesia, anesthesia if catheter anterior or lateral, hypotension	Paresthesia/ hypoesthesia, anesthesia if catheter anterior or lateral, hypotension	Delirium, dizziness, nystagmus, memory disorders, headaches, auditory hallucinations, drowsiness, blurred vision, nausea, vomiting	
Associations	Morphine Ropivacaine Ziconotide MRZ	Morphine Ropivacaine Ziconotide MRZ	Morphine Bupivacaine Ziconotide MBuZ	Morphine Ropivacaine Ziconotide MRZ	Morphine Bupivacaine Ziconotide MBuZ
pH of commercial solutions	Morphine 50 mg/mL pH = 3.4	Ropivacaine 10 mg/mL pH = 5.5	Bupivacaine 40 mg/mL pH = 5.7	Ziconotide 100 µg/mL pH = 5.1	
Presentations available in France	Morphine sulfate **50 mg/mL** ⇨ 500 mg - 10 mL Morphine hydrochloride **10 mg/mL** ⇨ 100 – 10 mL ⇨ 50 mg – 5 mL ⇨ 10 mg – 1 mL	Ropivacaine hydrochloride **10 mg/mL** ⇨ 200 mg – 20 mL **7.5 mg/mL** ⇨ 150 mg – 20 mL **2 mg/mL** ⇨ 400 mg –200 mL	Bupivacaine hydrochloride **40 mg/mL** ⇨ 200 mg – 5 mL	Ziconotide acetate **100 µg/mL** ⇨ 100 µg – 1 mL ⇨ 500 µg – 5 mL	

Less often, other treatments are used intrathecally, such as sufentanil, fentanyl and clonidine.

I.3 STABILITY DATA FOR INTRATHECAL DRUGS AND DRUG MIXTURES

- These are pharmacological data: the stability times given are thus valid only if the pharmaceutical preparation is identical to the prescription.
- This is important to know, because once this time has elapsed, although the preparation may still contain active ingredients, it may be less effective because their concentration has decreased (see graph Fig. 2 below). This must be taken into account in clinical practice.
- Classically, for a mixture of the three drugs morphine-ropivacaine-ziconotide in a SynchroMed II pump, the recommended duration of use in practice is 21 days.

Drug		Morphine	Ropivacaine	Bupivacaine	Ziconotide
Stability data	Syringe (polypropylene) [2]	Morphine sulfate 3.5 mg/mL Ropivacaine 7.5 mg/mL Ziconotide 1 µg/mL 2–8°C ⇨ **3 days**	Morphine sulfate 3.5 mg/mL Ropivacaine 7.5 mg/mL Ziconotide 1 µg/mL 2–8°C ⇨ **3 days**	No data found	Morphine sulfate 3.5 mg/mL Ropivacaine 7.5 mg/mL Ziconotide 1 µg/mL 2–8°C ⇨ **3 days**
	SynchroMed® II Medtronic* pump	Morphine sulfate or hydrochloride monotherapy 37 °C 25 mg/mL ⇨ **180 days[3]** Morphine sulfate Ropivacaine Ziconotide 12 mixtures studied 37°C ⇨ **[4]3.5 days** if pH < 4.5 ⇨ **13 days** if pH ≥ 4.5  Fig. 2. Mean ziconotide concentration loss in admixtures in Synchromed II at 37 °C. NB: The maximum concentration of morphine approved by Medtronic is 25 mg/mL	No data found	No data found	Ziconotide monotherapy 37 °C 100 µg/mL => **60 days** **57/158 days[5]** 25 µg/mL => **40 days** **13 / 53 days**
	Cassettes (PVC reservoir)	No data found	No data found	No data found	Ziconotide monotherapy 25 °C 0.4 µg/mL => **2 days[6]** 0.6 µg/mL => **2 days**

[2] J. Robert et al., "Chemical Stability of Morphine, Ropivacaine, and Ziconotide in Combination for Intrathecal Analgesia," Int. J. Pharm. Compd., vol. 21, no. 4, pp. 347–351, Aug. 2017.
[3] "Indications, drug stability, and emergency procedures SynchroMed and IsoMed implantable infusion systems." Accessed: Jun. 04, 2021. [Online]. Available: https://manuals.medtronic.com/content/dam/emanuals/neuro/M961294A015A_view.pdf
[4] C. Bazin, A.-L. Poirier, and D. Dupoiron, "Influence of pH and temperature on ziconotide stability in intrathecal analgesic admixtures in implantable pumps and syringes," Int. J. Pharm., vol. 487, no. 1– 2, pp. 285–291, Jun. 2015, doi: 10.1016/j.ijpharm.2015.04.041.
[5] D. E. Shields, W. Liu, K. Gunning, and R. Montenegro, "Statistical evaluation of the chemical stability of ziconotide solutions during simulated intrathecal administration," J. Pain Symptom Manage., vol. 36, no. 1, pp. e4–e6, 2008.
[6] J. Robert, J. Sorrieul, A. Andrieu, F. Mounsef, D. Dupoiron, and C. Devys, "Study of Physicochemical Stability of Ziconotide in Medication Cassette Reservoir," Neuromodulation Technol. Neural Interface, Jul. 2020, doi: 10.1111/ner.13218.

I.4 DECIDING ON THE INDICATION– MULTIDISCIPLINARY CONSULTATION MEETING

INDICATIONS FOR INTRATHECAL ANALGESIA (ITA)

- Patients **with intractable localized pain**[2],
- **Despite well-administered background treatment**, with morphine doses of around 300 mg/d in oral morphine equivalent,
- **Or adverse side effects** ruling out analgesics.
- For the following locations, early access to the technique is recommended:
    - Pelvic cancers or cancers with painful pelvic secondary sites
    - Pancreatic cancer, liver cancer
    - Pancoast-Tobias syndrome, or localizations with a strong neuropathic component
    - Hyperalgesic localized bone metastasis
    - Sarcomas
    - ENT cancer.

ABSOLUTE CONTRAINDICATIONS

- Intracranial hypertension
- Brain metastases with risk of herniation (brain imaging less than one month prior)
- Obstacle to CSF circulation in catheter path: spinal cord invasion or compressive vertebral fracture (recent spinal imaging).

TO BE DISCUSSED ON A CASE-BY-CASE BASIS (ANESTHETIST, NEUROSURGEON, ONCOLOGIST, ETC.)

- Aplasia, neutropenia, thrombopenia
- Hemostasis disorders, anticoagulant treatment not stopped
- Epiduritis (MRI useful),
- Infection
- Abdominal pocket not feasible (permeation nodules, stomas, ascites, etc.)
- Severe undernutrition
- Certain specific cancer treatments (notably bevacizumab).

[2] Deer TR, Pope JE, Hayek SM, Lamer TJ, Veizi IE, Erdek M, Wallace MS, Grider JS, Levy RM, Prager J, Rosen SM, Saulino M, Yaksh TL, De Andrés JA, Abejon Gonzalez D, Vesper J, Schu S, Simpson B, Mekhail N. The Polyanalgesic Consensus Conference (PACC): Recommendations for Intrathecal Drug Delivery: Guidance for Improving Safety and Mitigating Risks. Neuromodulation. 2017 Feb;20(2):155-176. doi: 10.1111/ner.12579. Epub 2017 Jan 2. PMID: 28042914.

COLLEGIAL DECISION MAKING

Prior process

The "referring" physician (oncologist, algologist, palliative care physician, supportive care physician):

- Examines the benefit/risk ratio considering the patient's overall situation, with the aim of improving quality of life,
- Informs the patient (and those close to the patient) about the analgesic technique,
- Presents the situation collegially.

COLLEGIAL DECISION AND/OR MULTIDISCIPLINARY CONSULTATION MEETING

Early multidisciplinary consultation (oncologists, radiotherapists, algologists, anesthetists, radiologists, palliative care specialists, attending physician, psychologist, nurse, etc.).

- Theoretical indication criteria validated,
- No formal contraindication to the technique at outset,
- **Feasibility established** (socio-familial, psychological, professional context, life prognosis, imaging assessment),
- **Other treatment options** (drug and interventional) **ruled out**,
- Coordination with outside caregivers and family (available in case of emergency),
- Choice of catheter positioning (see diagram),
- **For ENT/cephalic locations: contact trained teams for placement of cervical, cisternal +/- intracerebroventricular catheters and confirmation of indication.**

Choice of device based on:

- Life expectancy
- Relative contraindications (stomas, fistulas)
- Patient autonomy

I.5 INFORMATION FOR PATIENTS/CAREGIVERS

"Below is a proposed model information sheet for patients/careworkers. It does not replace the full, clear, fair, and appropriate information to be given to patients, including possible personalized alternatives, expected benefits, and any drawbacks and risks, with a view to obtaining free informed consent."

You have severe cancer pain, but the usual treatments have not relieved it or have had unwanted side effects.

As an alternative treatment, your doctor has suggested fitting a programmable implantable pump. This should give you greater relief and improve your quality of life.

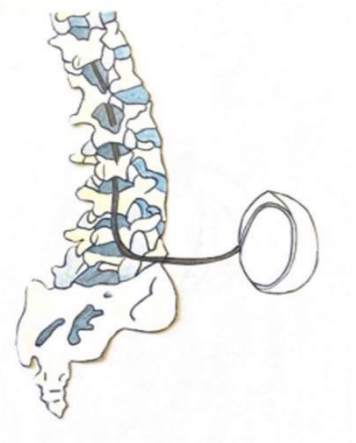
INTRATHECAL ANALGESIA:

WHAT IS IT?

A pump, placed under your skin, contains and dispenses painkillers.

This pump is connected to a thin flexible tube, called a catheter, which is also placed under your skin. It leads into the intrathecal space in your spine.

You'll have a remote control that communicates with the pump by radio waves. This lets you administer additional doses (called "boluses") when you feel pain. These doses are kept within the limits prescribed by your doctor, who programs all the treatment settings.



HOW DOES IT WORK?

The painkillers in the pump are delivered as close as possible to the nervous system. This way, they act directly on the nerve cells that send the pain message. This means doses can be much lower, so with fewer side effects.

HOW IS IT FITTED?

The pump and catheter are inserted surgically, under a general anesthetic. The procedure takes around 1 hour and needs a few days in hospital to set the treatment (on average 7 days).

AND AFTER THE SURGERY?

The pump is filled at intervals by the pain management team. They do this through a needle inserted through the center of the pump. This procedure is painless, but must be carried out in hospital, under conditions of maximum hygiene.

Pump programming (which sets the treatment doses) is reviewed and readjusted to your needs as necessary.

WHAT MUST I LOOK OUT FOR?

Contact your doctor or pain resource nurse if:

– The pain relief is insufficient,
– You have persistent side effects (drowsiness, hallucinations, etc.),
– There is redness or swelling around the implanted parts. Remember to tell your caregivers that injections into the abdomen are banned,
– You have a temperature or a headache,
– You are in the least doubt about the treatment.

IS IT COMPATIBLE WITH OTHER CARE? If you are fitted with an intrathecal analgesia pump:

- Imaging procedures (X-ray, CT scan, MRI, etc.) are possible with certain precautions. After an MRI scan, the pump must always be checked on the same day by a pain physician In all cases, tell the radiologist/radiographer that you are fitted with an intrathecal pump.
- Radiotherapy is still possible provided the pump is out of range In all cases, tell your radiotherapist that you are fitted with an intrathecal pump.
- All other surgical procedures are possible In all cases, inform the surgeon that you are fitted with an intrathecal pump.

LIVING WITH THE PUMP: if in any doubt, consult your doctor.

- Always have the pump identification card on you and show it to all healthcare professionals who need to treat you.
- Avoid physical activities that could affect the area where the pump or catheter is implanted. Avoid excessive twisting or stretching around the pump. Avoid wide temperature changes (consult your doctor before flying or hiking at altitude).
- Diving: do not dive beyond a depth of 10 m or enter a hyperbaric chamber exceeding 2 absolute atmospheres.
- Rule out hot tubs, saunas, steam baths, and solariums.

II.1.A IMPLANT/PRE-OPERATIVE PHASE: CHOICE OF OPERATING DATE – PATIENT PATHWAY AND ONGOING CHEMOTHERAPY

EXAMINATIONS REQUIRED

All the information must be recorded in the consultation report.

1. Consultation for anesthesia

Including basic blood work

- CBC-platelets (PNN must be > 500/mm^3 and platelets > 80,000/mm^3),
- Coagulation workup : TP/TCA, INR,
- Blood group,
- *To be discussed with anesthetist:* blood ionogram.

2. Managing anticoagulants (example given with help of French recommendations):

Cessation and relaying follow four main principles:

- Multidisciplinary discussion with medical and surgical operators,
- Benefit/risk ratio assessment for each patient, with the help of relevant national recommendations,
- Placement of a long-term intrathecal catheter should be treated as axial neurosurgery,
- Hemostasis and platelets must be checked the evening before for all anticoagulant treatments.

Heparins	Last administration	Resumption
LMWH fractionated		
Curative	H-24	According to departmental protocol
Preventive	H-12	
LMWH non-fractionated		
Curative IV pump	H-4–H-6	According to departmental protocol
Preventive SC	H-8–H-12	
Platelet inhibitors	**Last administration**	**Resumption**
Acetylsalicylic acid		
< 100 mg	Continuous	According to departmental protocol
> 100 mg	D-3	
Clopidrogel and ticagrelor	D-5	According to departmental protocol
Prasugrel	D-7	According to departmental protocol

Surgery with high risk of bleeding and thrombosis	What to do						
	D-6	D-5	D-4	D-3	D-2	D-1	D0
VKA	+	+	-	-	-	-	-
LMWH	-	-	-	+	+	+	-
High risk of thrombosis: AF with stroke, VTE < 3 months PE < 3 months, thrombophilia under VKA, mechanical valves							
Surgery with high risk of bleeding and thrombosis and RI or age > 75 years	**D-6**	**D-5**	**D-4**	**D-3**	**D-2**	**D-1**	**D0**
VKA	+	+	-	-	-	-	-
LMWH	-	-	-	-	-	-	-
Surgery with high risk of bleeding without risk of thrombosis	**D-6**	**D-5**	**D-4**	**D-3**	**D-2**	**D-1**	**D0**
VKA	+	-	-	-	-	-	-
LMWH	-	-	-	-	-	-	-

*** CHADSVASC-2 score:**

- 1 point if age 64–75 years, HBP, diabetes, female, LV dysfunction
- 2 points if history of stroke/TIA, age > 75 years

VKA prescribed for AF according to CHADSVASC-2* score	What to do									
CHADSVASC-2 ≤ 5	**D-6**	**D-5**	**D-4**	**D-3**	**D-2**	**D-1**	**D0**	**D+1**	**D+2**	**D+3**
VKA	+	-	-	-	-	-	-	-	-	-
ENOXAPARIN	-	-	-	-	-	-	+p	+p	+p	+c
HEMOSTASIS						PT evening				

VKA prescribed for AF according to CHADSVASC-2* score	What to do									
CHADSVASC-2 > 5	**D-6**	**D-5**	**D-4**	**D-3**	**D-2**	**D-1**	**D0**	**D+1**	**D+2**	**D+3**
VKA	+	-	-	-	-	-	-	-	-	-
ENOXAPARIN	-	-	-	$+_c$	$+_c$	+c morning	$+_p$	$+_p$	$+_p$	$+_c$
HEMOSTASIS						PT even ing				

p: preventive, c: curative

DOA (direct oral anticoagulant)	What to do						
	D-6	**D-5**	**D-4**	**D-3**	**D-2**	**D-1**	**D0**
APIXABAN – RIVAROXABAN - DABIGATRAN	DOA	DOA	-	-	-	-	-

3. Assess the risks of slow healing

– Albumin nutritional assessment (possible costing of stay and planning for any healing difficulties in cases of undernutrition),

– Blood glucose monitoring,

– Tobacco,

– Corticoids,

– Anti-angiogenic agents.

4. Imaging to be redone if necessary (see Worksheet 1.4)

5. What to do about ongoing medication

– Stop or reduce *corticoids*

- Objective: find the smallest dose necessary and sufficient for the patient

– *Analgesics:*

- Complete list of ongoing medication,
- Opioids: relay strategy to be determined, see Worksheet II.3.

– *Other treatments:*

- *Oncological treatments:* To be discussed with oncologists:
  - Chemotherapies: Stop at least 15 days before procedure and resume 7–10 days if healing is satisfactory.
  - Immunotherapy: No foreseeable complications related to the procedure.
  - Tyrosine kinase inhibitors: No foreseeable complications related to the procedure except for
    - Those with an anti-angiogenic action (axitinib, sunitinib, pazopanib, regorafenib, lenvatinib).
  - Anti-angiogenic agents: bevacizumab
    - Stop at least three weeks before implantation and resume 15 days to three weeks later, provided healing is satisfactory.

6. Patient information booklet (Worksheet I.5)

7. Choice of operative date if not set at time of collegial decision

8. Informed consent

II1B. PRESCRIPTION FIRST SYRINGE

CHOICE OF DRUGS

International PACC recommendations (Polyanalgesic Consensus Conference 2017)[3]

First line	**Morphine + bupivacaine**	Ziconotide	Morphine		
Second line	**Morphine + ziconotide**	Morphine + clonidine			
Third line	**Morphine/fentanyl + bupivacaine + ziconotide**	Morphine/fentanyl + bupivacaïne + clonidine	Ziconotide + bupivacaïne	Ziconotide + clonidine	Sufentanil

As practiced in France :

First line	**Morphine + local anesthetic local (ropivacaine) + ziconotide**	**Morphine + local anesthetic (ropivacaine) (if ziconotide unavailable)**

- Prescribing ziconotide also depends on the compounding pharmacy (it must be available and safely prepared). However, note that the sooner ziconotide is introduced, the better tolerated it will be, as increases can be made very gradually.

Determination of initial daily doses

- Morphine: 1/100 dose IV/day = 1/300 dose orally/day (do not exceed 5 mg/24 h),
- Ropivacaine: 6–8 mg/day
  ➔Initial dosage according to catheter level (if cervical, better 6 mg/24 h; if low thoracic, better 8 mg/24 h),
- Ziconotide = 0.25–0.5 µg/day
  ➔Initial dosage according to catheter level (if cervical, better 0.25 µg/24 h; if low thoracic, better 0.5 µg/24 h).

Setting flow rates

- On intrathecal drug delivery system (IDDS): start flow rate at 1 ml/day.
- On external pump, intrathecal site (ITS): start flow rate at 4.8 ml/day, i.e., 0.2 ml/h on syringe
- pump.
  ➔These round figures make it easier to calculate flow rate adjustments during the first few days of hospitalization.

[3] -Deer TR, Pope JE, Hayek SM, Lamer TJ, Veizi IE, Erdek M, Wallace MS, Grider JS, Levy RM, Prager J, Rosen SM, Saulino M, Yaksh TL, De Andrés JA, Abejon Gonzalez D, Vesper J, Schu S, Simpson B, Mekhail N. The Polyanalgesic Consensus Conference (PACC): Recommendations for Intrathecal Drug Delivery: Guidance for Improving Safety and Mitigating Risks. Neuromodulation. 2017 Feb;20(2):155-176. doi: 10.1111/ner.12579. Epub 2017 Jan 2. PMID: 28042914.

Setting bolus dosages

- The patient can be offered the option of bolusing with a remote control to administer an additional dose when pain peaks. Remember to tell the patient that an intrathecal bolus is very different from an intravenous bolus, with different sensations (no "shoot" effect) and a longer duration of action.

  Bolus: 1/24 (often at ITS for a bolus at 0.2 ml, maximum round figure to avoid errors) at 1/10 daily dose (with IDDS)

  Refractory period: 1 h

  Number of boluses authorized often 10–12/24 h at first fill.

Example

Mr X presents with refractory pelvic and lower limb pain associated with secondary lesions of a prostatic adenocarcinoma. Insufficiently relieved by morphine hydrochloride sustained release (MSR) 200 mg morning and evening + 5 interdoses of morphine hydrochloride immediate release (MIR) 40 mg.

First syringe: OME (oral morphine equivalent) = 600 mg

➔ Morphine IT = 600/300 = 2 mg/24 h

➔ Ropivacaine IT (low pain, low thoracic catheter) = 8 mg/24 h

➔ Ziconotide IT (low pain, low thoracic catheter) = 0.5 µg/24 h

Prescription calculator

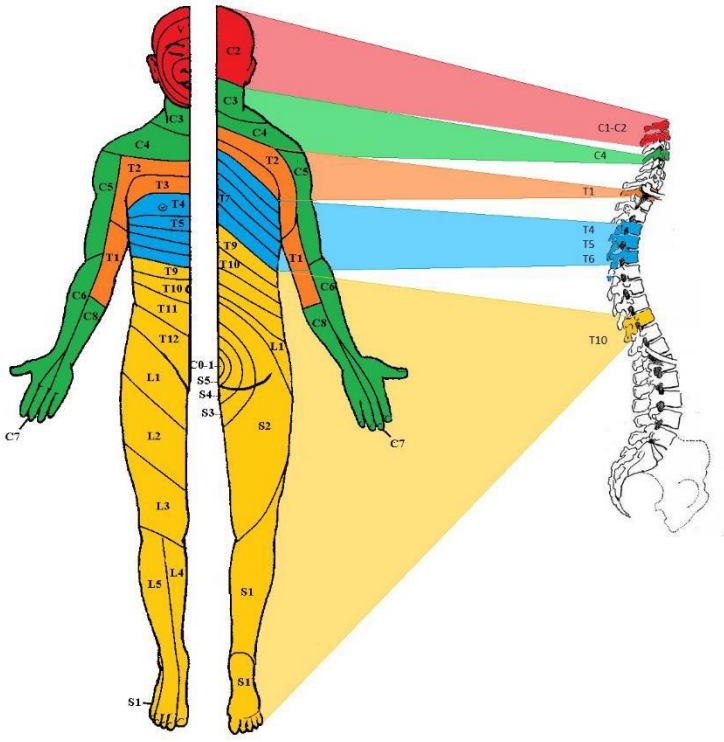
Patient safety must remain the priority. Hand-written prescriptions on plain paper must be avoided, especially if mixtures are used. They can be a source of error and risk of overdosing.

- Tools on a hospital's secure server are to be preferred ++,
- The calculator must be shared or there must be communication with the pharmacy,
- Avoid as much as possible all prescription tools where calculations can easily be changed by mistake,
- Remember identity vigilance: last name, first name, date of birth, file number, to avoid prescription errors.
- Store prescriptions to keep a history and a reference for subsequent prescriptions.
- Prescriptions must be traceable, with date of prescription, date of filling, and prescribing doctor.

For greater security, some facilities require two prescribing physicians to sign prescriptions.

II.2 SURGICAL TECHNIQUE

- General anesthesia,
- Patient in lateral decubitus position (on the side contralateral to the side chosen for the pump installation),
- Scopic location of catheter positioning level
    - Scopy must not only show the corresponding vertebral level, but also ensure that the catheter is correctly positioned behind the spinal cord (strict profile).
- Antibiotic prophylaxis 30 min before incision: cefazolin 2 g or vancomycin if allergic,
- Location of two incisions – abdominal para-umbilical or supra-gluteal region, lumbar centered on L3-L4 or L2-L3 (ultrasound can help to locate the various anatomical landmarks for puncture),
- Asepsis, sterile drapes placed so that the tunneling path is visible to avoid skin damage along the path,
- Linear incision on the line of the spinal processes centered on the L3L4 or L2L3 space.
- Opening of subcutaneous space to make room for connectors,
- Lumbar puncture using a 16G Tuohy needle (needle at 30° lateral to the line of the spinal processes to prevent the catheter from running out ventrally),
- The catheter (4-layer for compression strength) is inserted into the intrathecal space to the desired level with scopy.



    - D10-D11 for subdiaphragmatic pain
    - D2-D3 for chest pain
    - D4-D6 for epigastric/pancreatic pain
    - C3-C5 for upper limb pain
    - C1-Cisternal for ENT and facial pain

- Removal of guidewire and 16G Tuohy needle
    - Only the distal end of the catheter remains radiopaque after guidewire removal,
- Fixation of the catheter to the lumbar fascia using the appropriate device,

- 7–8 cm linear incision in the para-umbilical or supra-gluteal region
    - Subcutaneous pocket to accommodate pump,
    - For very low-weight patients, the pump position can be subaponeurotic,
    - If abdominal location is impossible (e.g., double stoma), use supra-gluteal location,
- Tunneling between the two incisions,
- Irrespective of catheter model, connection at either lumbar or abdominal/gluteal level:
    - Remember to measure the final length of the catheter before programming the pump (the length actually implanted will be entered),
- Catheter priming to ensure CSF reflux,
- CSF sample sent for anatomopathological and bacteriological analysis,
- The pump, filled by the manufacturer with physiological saline, is emptied by drawing off the saline through the central valve with the filling kit needle,
- Filling with the analgesic preparation via the same access site,
- Connection of the pump to the catheter,
- Positioning of the pump in the abdominal/gluteal pocket:
    - Avoid placing the central valve opposite the incision site to reduce the risk of infection and pain during filling,
    - Position the pump tip according to the team's routine to make it easier to locate the pump when filling (e.g., at 10 o'clock), but not too close to the ribcage to avoid discomfort when the patient is seated,
    - Make sure the catheter has no loops in front of the pump to avoid puncturing the catheter when filling.
- Secure the pump to the abdominal fascia with lateral anchors,
- After the surgery, program the pump with:
    - Patient data,
    - Drugs, with their concentration in the mixture:
        - Note that the concentrations are those in the mixture and not the initial concentrations of the drugs,
    - Length of the catheter,
    - Priming bolus,
    - Remote control programming - bolus frequency, number and volume.
- Total surgery time < 1 hour.

II.3 IMMEDIATE POST-OPERATIVE PERIOD

PLACE OF HOSPITALIZATION

- Close monitoring in a continuing care unit for 48 hours required, if available, or failing that in a unit with staff trained in monitoring dressings, withdrawal syndrome, post-PL headache, and remote control use,
- Close monitoring, e.g., every 2 hours for 12 hours, then every 4 hours for 12 hours, then once per shift,
- In all cases, allow an average of 7 days' hospitalization.

PATIENT ASSESSMENT AND MONITORING :

- As with all pain symptoms, a complete pain assessment must be made:
  - Location: Is it old pain? New pain? Scar pain?
  - Efficacy of treatments: Intrathecal boluses (morphine + AL +/- ziconotide) are classically effective >15 minutes (depending on bolus administration rate). NB: bolus effective in 1 minute = placebo effect,
  - Adverse effects: Withdrawal syndrome, post-LP syndrome, adverse drug reactions?
- If imaging is available: schedule a postoperative CT scan to check catheter positioning.

Patient education, listening to the patient, caregiver/patient relation :

- Educate patients about the need for boluses when adapting treatment, as some patients avoid boluses for fear of adverse effects (as with oral treatment).
- Conversely, some patients only feel well with 8 systematic boluses, and do not wish to change the basal rate, hence the importance of discussion with the patient.

➔ Treatment is individualized.

Adaptation of treatments (outside intrathecal treatments)

Postoperative pain:

- Use of paracetamol +/- continuous or discontinuous nefopam (80 mg/24 h syringe pump or 20 mg/administration for 2–3 days),
- Cold physiotherapy,
- Intrathecal boluses are often ineffective against these symptoms.

Oral/systemic treatments:

- Complete immediate opioid weaning in the recovery room, or
- Gradual weaning: there are several protocols, depending on the team's routine,
  - ➔ In all cases, complete weaning from oral/systemic opioids is recommended at discharge,
- Wean off other analgesics also: anti-epileptics, antidepressants for neuropathy, etc.

Monitoring

Monitoring of withdrawal syndrome:

- Sweating, irritability, diarrhea, nausea, insomnia, agitation, etc.
- *Treatment: syndrome often improves without treatment:*
    - For severe and persistent syndromes: use benzodiazepines or clonidine (50 g over 1 hour then 150 g over 24 h IV syringe pump,
    - Symptomatic treatments: if nausea, anti-emetics, etc.

Monitoring of post-PL syndrome:

- Symptoms include postural headache +/- stiff neck +/- nausea +/- vomiting +/- diplopia/transient hypoacusis.
- May be mitigated by use of biocompatible sealing during implantation at catheter puncture point.
- *Treatment:*
    - Hydration, antiemetics, gabapentin and theophylline,
    - If persistent: brain imaging (preferably MRI) to look for subdural laminae indicating intracranial hypotension,
    - Exceptionally, blood patch (risk of infection during the procedure and damage to the spinal portion of the catheter).

Adaptation of intrathecal treatment D1 (Worksheet II.1.b)

- NB: there are no clear rules to be found in the literature, but some suggestions can be made:
- Increase intrathecal treatments cautiously in the first 24 hours, as symptoms are diffuse between post-op and weaning, unless the patient is hyperalgesic.

Likewise, if the patient is very drowsy and non-algesic, check pump settings, discuss additional imaging (catheter positioning and search for subdural hematomas) and lower intrathecal doses, including in the first 24 hours.

From D2

- Whenever possible, for a better assessment, wait 24 h between changes before readjusting dosage,

- Depending on the number of boluses performed:

Between 4 and 6 boluses per day

- The equivalent of 2 boluses is included in the background dose, i.e., an increase of 20%.

More than 6 boluses per day

- The background dose includes the equivalent of 3 boluses, i.e., an increase of 30%.

if <4 boluses per day while gradually resuming activities

- There is no need to increase the background dose during this phase (but perhaps during the HDJ filling phase)

If drowsiness +++ and perfect analgesia

- On the contrary, plan to reduce IT doses (by between 20 and 30%). Continue to reduce if symptoms persist.
- NB, if there is a resurgence of pain after this reduction, plan a new filling with an isolated reduction in morphine and leave the local anesthetic and ziconotide at the previous doses. Cf specific Worksheet IV.3 What to do about treatment-related adverse events.

II.4 DISCHARGE OF PATIENT FITTED WITH AN IMPLANTED INTRATHECAL PUMP

SCHEDULED APPOINTMENTS:

- Date of next assessment (within 10 days of discharge),
- Date of next pump filling,
- Date of suture removal (if non-absorbable).

DOCUMENTS TO BE GIVEN TO THE PATIENT BEFORE DISCHARGE:

- Pump identification card to be carried by the patient,
- Pain assessment logbook to be completed by the patient, if necessary,
- Letter to attending physician and oncologist,
- 24/7 pain management hotline,
- Wound dressing prescriptions for home care nurse and lidocaine/prilocaine patch (for next refill).

REMINDER OF THE WARNING SIGNS FOR THE PATIENT THAT CALL FOR A NEW ASSESSMENT (SEE WORKSHEET IV.2):

- *Digestive signs:* nausea, vomiting, constipation
- *Urinary signs:* dysuria
- *Infectious signs:* fever, headache, stiff neck
- *General signs:* worsened general condition, asthenia, drowsiness
- *Pain signs:* changes in pain intensity or characteristics
- *Psychic signs:* depression, hallucinations, anxiety, agitation, delirium.

REVIEW USE OF THE REMOTE CONTROL WITH THE PATIENT (WORKSHEET V.3)IF USING CONTINUOUS +BOLUS MODE (+ ADVISE THE PATIENT TO CARRY IT AT ALL TIMES).

SEE: DOCUMENTS FOR PATIENT /CAREGIVERS

RECOMMENDATIONS

Recommendations for the patient

- Avoid twisting your body.
- Avoid lying on your front.
- Avoid raising your arms above your head.
- Avoid scuba diving.
- Avoid hot baths, steam rooms, and saunas.

Recommendations for caregivers (see Worksheets V):

- Never stop the pump.
- Never make SC injections in the abdomen.
- Never irradiate the implanted pump.
- Remember to check the pump after MRI.
- If a lumbar puncture is needed, think about the operating orifice.
- Know what to do if there is pain, a collection, or poor healing.
- At end-of-life, consider home refilling.
- In the event of death, use specific procedures.

III.1 POST-IMPLANT PHASE: FOLLOW-UP OF PATIENT, REFILLING AND RE-PROGRAMMING THE PUMP

Players	Stages		File traceability
Doctor + nurse	Clinical assessment before filling date (can be done by telephone)	• Clinical assessment of the patient: EN, adverse effects, repercussions, quality of life • Prescription written on calculator • Sent to pharmacy	Follow-up telephone report on file Duplicate prescription
Preparer Pharmacy	Preparation of intrathecal treatment (syringe) in a fume hood		Traceability Pharmacy
Doctor + nurse	Clinical assessment at the patient's bed and Filling the pump	• Clinical assessment of the patient • Consultation between doctor and nurse • Draining/Filling • /Pump reprogramming • Double check of programming • Date of next filling	Reporting, day hospital, filling
Secretariat	Scheduling appointments in the department (diary)		

III.2.A. ASSESSMENT PRIOR TO REFILLING AN INTRATHECAL PUMP

BEFORE REFILLING (ACCORDING TO THE ORGANIZATION OF THE DEPARTMENT AND OF THE PHARMACY: SET DAY?24 H TO 48 H BEFOREHAND?)

Can be done by phone

- Introduce the caregiver: doctor or pain referral nurse.
- Reminder of filling date: ……
- Accompanied or unaccompanied patient, **suitable means of transport.**
- Patient's IDDS follow-up logbook, to be brought along if the patient has it.
- **Pain intensity** using a validated tool: VAS/VRS/NRS, at rest, on mobilization.
- Assessment of **efficacy** of IDDS on pain: % improvement in pain scores.
- Assessment of **quality of life and functional impact.**
- **Number of painful episodes** reported in a patient's typical day.
- **Enough sleep**? yes? no?
- **Number of boluses performed if authorized**? Effectiveness of boluses? In what timeframe?
- **Drug tolerance**: Any adverse effects (confusion, drowsiness, hallucinations, memory disorders, sensory/motor disorders, etc.)?
- **Any questions** from the patient.
- **Traceability** of the assessment in the patient file.

Evaluator's role: prescribing or passing on data to the prescriber for that purpose.

BEDSIDE CLINICAL ASSESSMENT OF THE PATIENT (FILLING DAY)

- **Pain intensity** using a validated tool: VAS/VRS/NRS,
- Evaluation of the **effectiveness** of the IDDS on pain: % improvement in pain scores,
- Assessment of **quality of life and functional impact,**
- **Number of pain episodes** reported in patient's typical day,
- **Number of boluses actually taken.** If different from initial assessment, plan patient education.
- **Drug tolerance**: any adverse effects? Overdosing? (confusion, drowsiness, sensory/motor disorders, etc.),
  - ➔ Programming as initially planned or modification thereof +/- new prescription (if changes between initial assessment and on the day of filling),
- **Recording of vital signs,**
- **Healing** at the implant site: pain, redness, wound opening, etc. (see Worksheet V.5),
- Fill in IDDS follow-up logbook,
- **Organize discharge**: date of next follow-up phone call / date of next refill.

III.2.B PRESCRIPTION FOR REFILLING

Reminder:

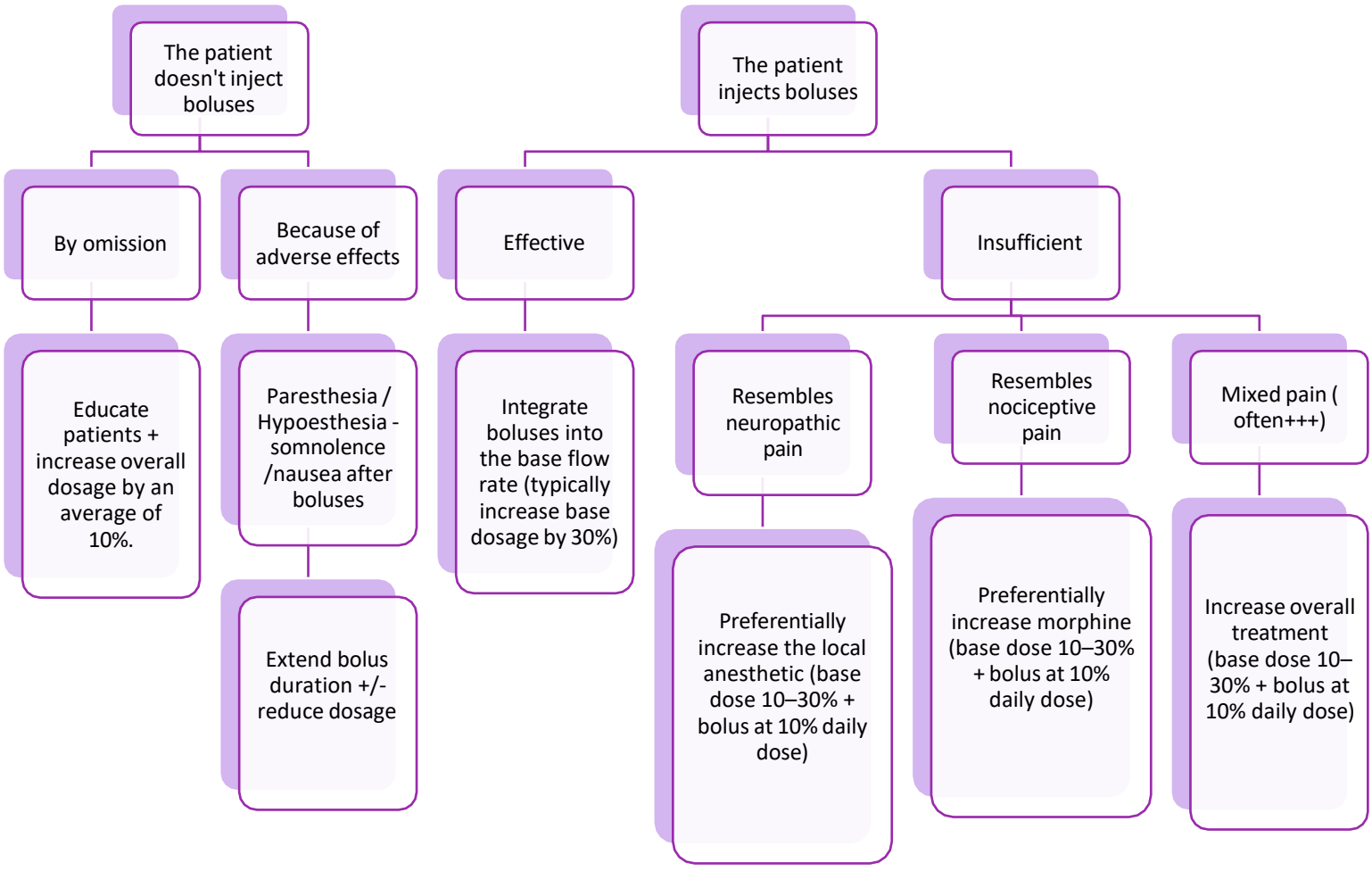
"There is no clearly established consensus, but a few guidelines are offered to help with prescribing. Prescribing remains the responsibility of the prescribing physician and is discussed according to each patient's specific clinical picture."

After assessment a few days before refilling, there are several possible situations:

ANALGESIA IS SATISFACTORY, NO UNWANTED SIDE EFFECTS

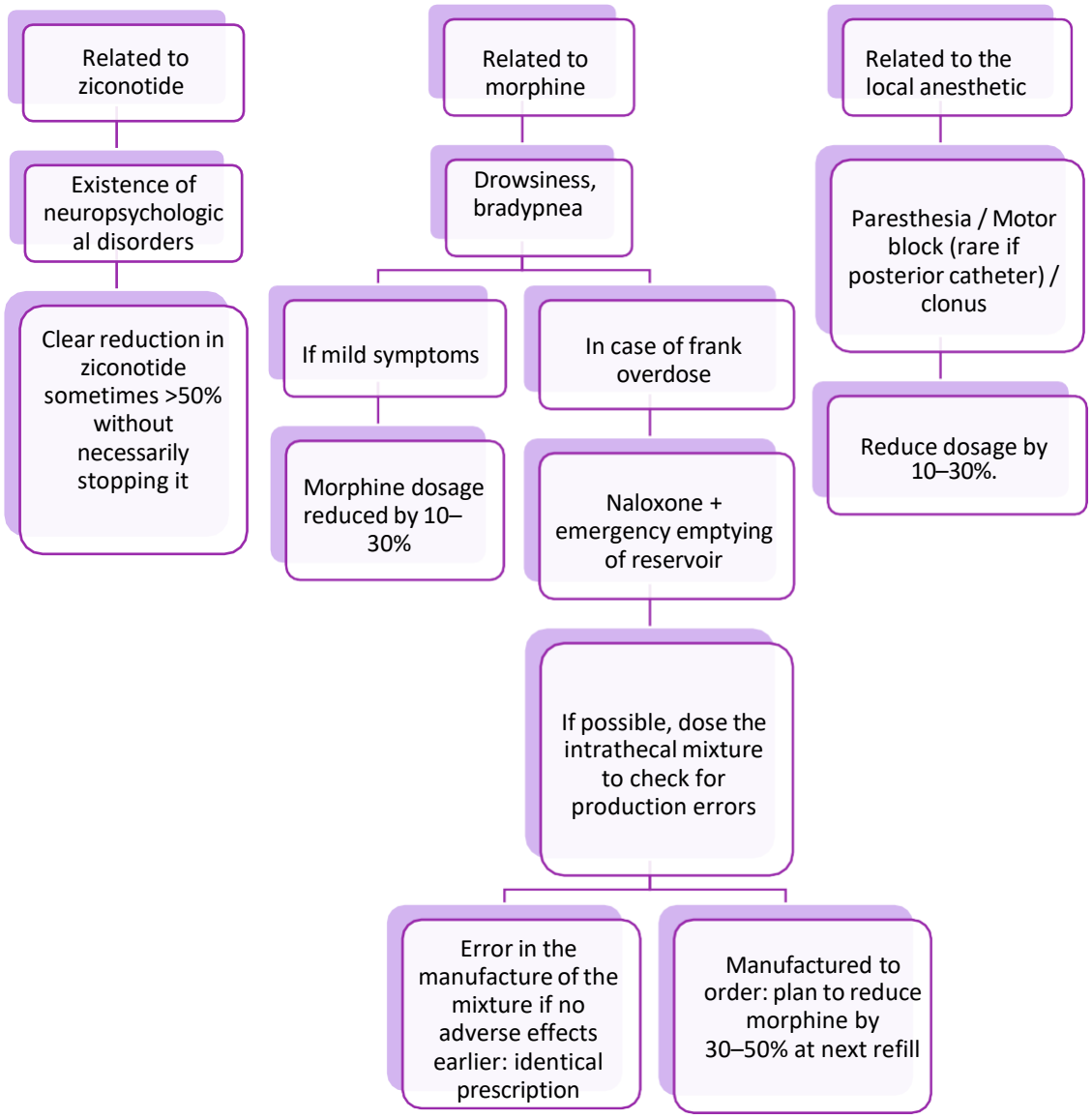
- Find the lowest effective dosage.
- Increase ziconotide very gradually to seek a co-analgesic effect (0.1–0.2 g/24 h regularly at different fillings until well tolerated (max recommended: increase of 0.5 g/24 h per week)).
- Adapt the number and dose of boluses /24 h to increase the filling interval.

ANALGESIA IS INSUFFICIENT



- Increase the number of authorized boluses, at least temporarily, to restore equilibrium.
- As pain is of mixed type in most cases, all treatments should be increased at the time of filling to maintain a satisfactory morphine/local anesthetic ratio (e.g., not 30 mg morphine for 10 mg ropivacaine, but ideally a ratio of 1(morphine)/6 (ropivacaine))
- NB: Owing to the large volume of ropivacaine (10 mg/ml), its increase can sometimes be limited, as it greatly shortens the interval between successive fillings. Hence the usefulness of the co-analgesic ziconotide, increased regularly, which can take over, or a switch to concentrated bupivacaine (40 mg/ml).
- Verification of correct catheter position, if in any doubt, by imaging with 3D reconstruction and/or correct pump operation.

ADVERSE EFFECTS ARE FOREMOST IN MIND



III.3 REFILLING / PROGRAMMING

MATERIALS REQUIRED

- 1 sterile gown
- 3 scrub caps minimum (for patient + nurse + helper)
- 3 masks (for patient + nurse + helper)
- 1 bin bag, 100 L
- 1 small needle box
- 1 fenestrated drape, 98 × 150 cm
- 1 table drape, 190 × 140 cm
- 1 filling kit
- 2 pairs of sterile gloves
- 5 packets of sterile swabs
- 1 small dressing
- 1 dose of povidone-iodine surgical scrub
- 1 dose of sterile water
- 2 doses of alcohol-based dermal povidone-iodine.

PROCEDURE

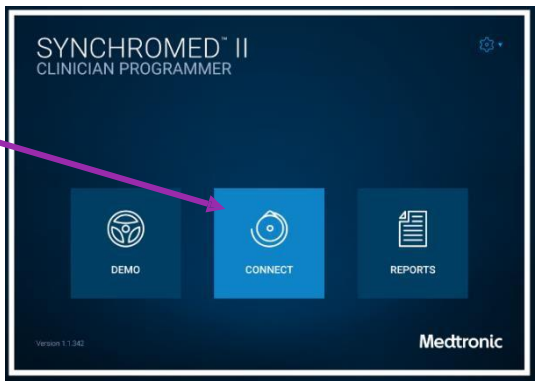
Verify patient's identity.

Install patient.

Assess pain and treatment side effects.

For example, query pump with tablet and wireless communicator

- Open the SynchroMed II application,
- Touch <connect>,
- Place the communicator on the implanted pump:



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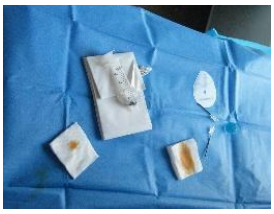
- The progress of the communication is displayed.
- The home screen is displayed with current settings.
- Note the residual volume.
- Note the number of successful activations.

Safety

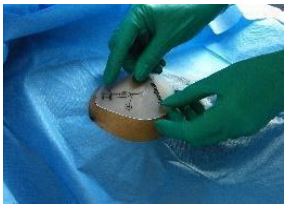
- Check syringe data against computer prescription +/- calculator (if two different tools are used) (last name/first name/date of birth/ patient number/names of drugs and their concentrations).
- Stick the syringe label on the paper prescription (note on the label: date, name + signature).

Refilling: procedure

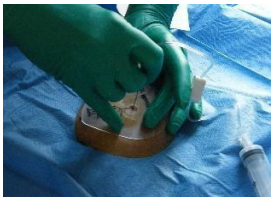
- Disinfect work surface and place bin bag. Caregivers and patient don mask and scrub cap,
- Place the patient supine.
- Remove local anesthetic patch (e.g., lidocaine/prilocaine) if present. Apply equimolar oxygen/nitrous oxide gas if necessary.
- Rub with alcohol-based solution.
- Disinfect in 3 steps in a circle from the puncture point outwards.
- Rub with alcohol-based solution.
- Nurse dons sterile gown and sterile gloves.
- 4th disinfection step.
- Put in place the sterile fenestrated drape and the table drape. Change gloves if de-sterilized.



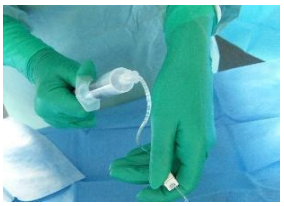
- **Place on the sterile drape the components of the specific IDDS set (Medtronic ref: 8551) + syringe** presented aseptically by the care helper. Fit the empty syringe in the Medtronic set with the tubing and needle clamp closed, to remove the residual volume.



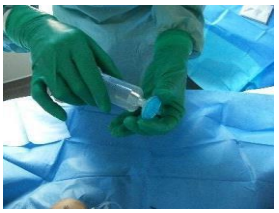
- **Place the template on the patient's IDDS pocket so that it fits its shape.**

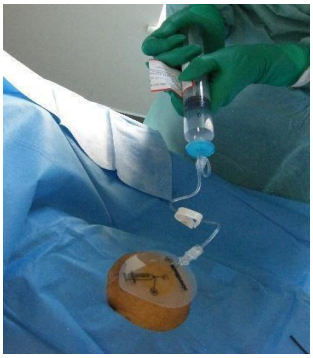


- **Insert the needle at a right angle.**
- **Open the clamp and aspirate the residual volume until air bubbles appear in the tubing. Clamp.**
- **The aspirated volume must equal the residual volume read when the pump was queried (+/- 15%).**



- **Fit the 0.22 filter to the syringe containing the analgesic drugs (syringe filled at the pharmacy).**
  - Remove the syringe used for purging. Fit the syringe containing the analgesics with sterile swabs soaked in alcohol-based antiseptic.





- **Open the clamp and gently inject (max 1 ml/3 sec) the contents of the syringe into the pump.**
- Clamp tubing, remove needle. Remove template.
- Apply antisepsis. After drying, apply a dry occlusive dressing for 24 hours.
- Remove sterile drape and gloves.
- Resettle the patient and remove patient's scrub cap.
- Rub with alcohol-based solution.

Programming

Follow the tablet instructions by scrolling through the following screens in turn:

PATIENT INFORMATION> SCREEN

- Select the input field or on the drop-down list.
- Enter or select information.
- Touch the <hide keyboard> button to hide the keyboard when you have finished.

<PUMP INFORMATION>SCREEN

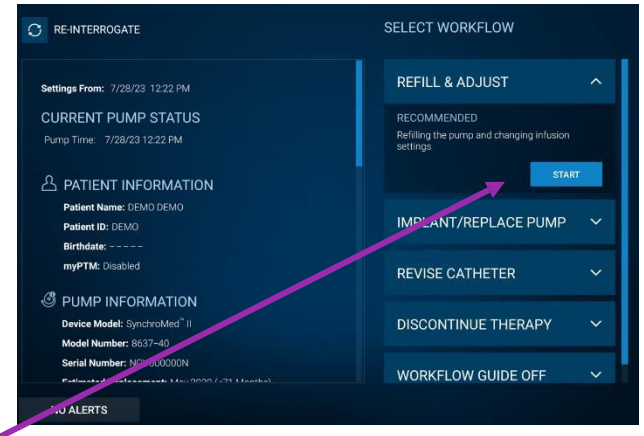
- Contains detailed pump information (name, volume, serial number).

CATHETER INFORMATION SCREEN

- Touch the drop-down list of catheter model numbers.
- Select the catheter model.
- Touch the implanted catheter volume input field.
- Enter the necessary information.
- Touch the confirm button.

<REFILL AND ADJUST> SCREEN

- Touch <start> to make new settings.



DRUGS TAB

1. To modify or add a drug entry:
   - Touch the <modify> button in the drug entry field or the <add drug> button.
   - Modify or enter the drug name.
   - Select a unit from the drop-down list.
   - Touch the <concentration> input field.
   - Touch the <confirm> button.
2. To delete a drug entry:
   - Touch the drug entry field.
   - Touch the <delete drug> button

RESERVOIR TAB

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1. To change the reservoir volume:
- Touch the <change> button in the <reservoir volume> input field,
- Enter a volume within the specified range or drag the arrows on the pump image to the appropriate level,
- Touch <confirm>.

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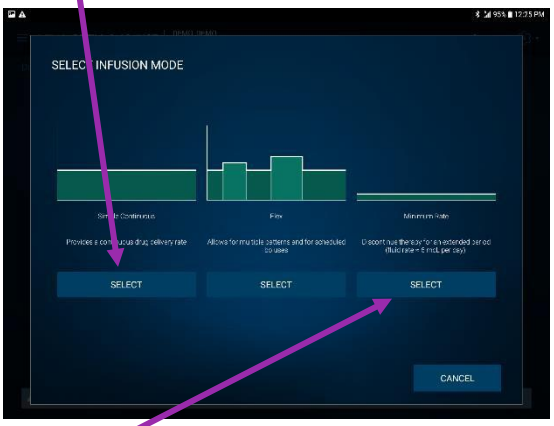
INFUSION TAB

1 To change the infusion mode:

- Touch the <change> button next to the infusion mode name,
- Touch the <select> button under the desired infusion mode. In principle, the <simple continuous> mode is the one used. It administers a continuous infusion of the dose specified per day.



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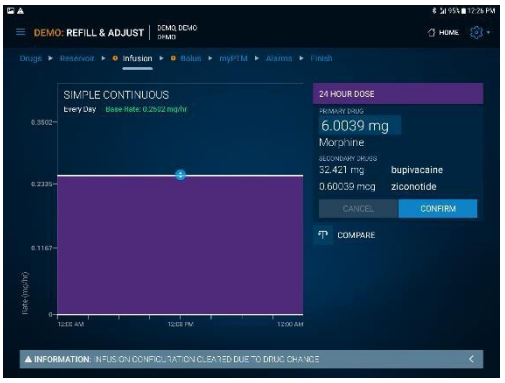
Select the <minimum rate> mode to stop the infusion: the drug will then be administered at a rate of about 0.006 ml/day.

- Touch <change mode>,
- Enter the desired dose per 24 h using the keypad or by dragging the arrows on the infusion display,
- Touch <finish>,
- Check the information and touch <confirm>.

2. To change the dose per 24 h:

- Touch the <change> button on <dose over 24 h>,
- Select the <main drug> input field and enter the new value using the keyboard,
- Touch <end>.



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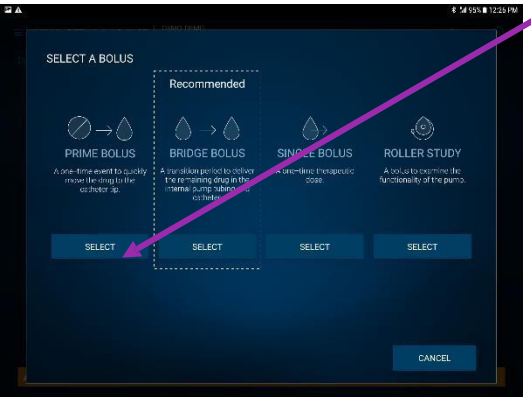
BOLUS TAB Choose the type of bolus you require (see Bolus Worksheet for bolus type information V.2)



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1. Prime bolus
- Check drug location,
- Touch the <start configuration> button,
- Answer each question in the scenario,
- Select each answer and then touch <next>,
- When you have answered all the questions, confirm the drug locations using the image of the reservoir and pump tubing,
- Touch <next>. The programmer will calculate a bolus volume and duration according to the answers given to the scenario,
- Touch <confirm>.

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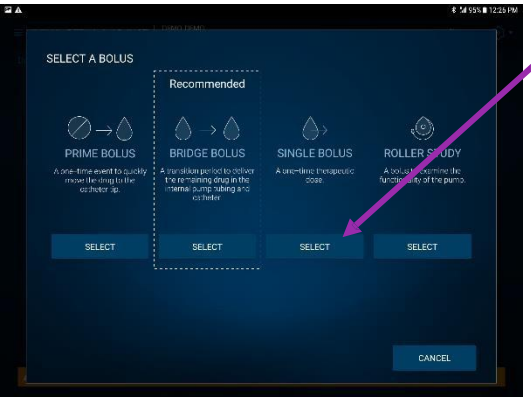
2 Bridge bolus
- Touch the <start configuration> button,
- Use the arrow buttons to select the <24 h dose during bridge> value,
- Touch the <next> button,
- Check bolus settings,
- Touch <confirm>.



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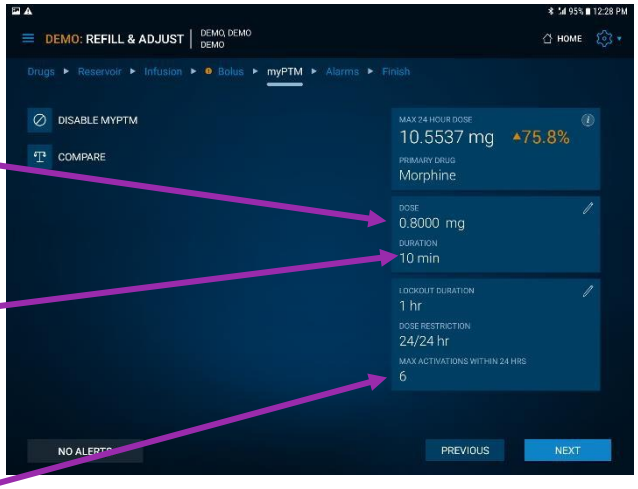
3 **Single bolus (= Physician bolus)**
- Touch the <new bolus> button,
- Touch the <select> button under <single bolus>,
- Enter the dose,
- Enter the duration (minimum default duration shown on the tablet),
- Enter the number of boluses per day,
- Touch <confirm>.

myPTM TAB (PATIENT BOLUS)

To program the administration of patient boluses:

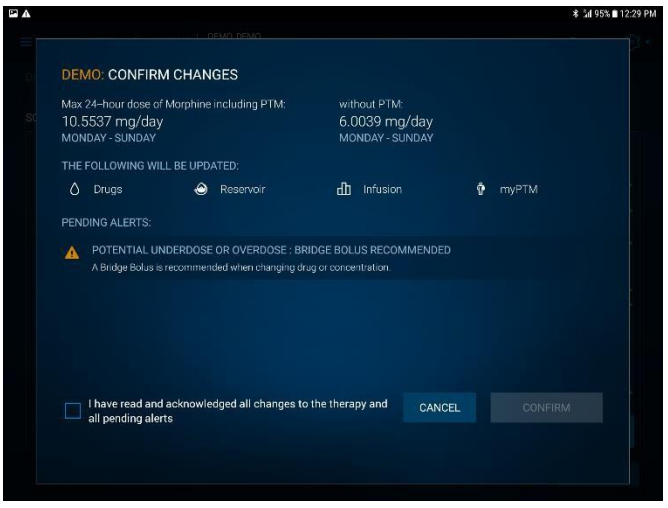
- On the myPTM screen, touch the <activate myPTM> button.
- Enter the dose activated by the patient.
- Touch the <confirm> button.
- Check the default dose and duration values in <dose and duration> and make any necessary adjustments.
- Touch <confirm> to move on to set patient restrictions.
- Set lockout duration.
- Select maximum number of activations.
- Select max activations within 24 h.
- Touch <confirm>.

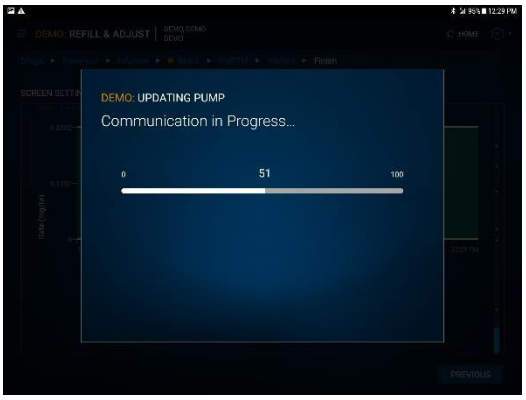


ALARMS TAB summarizes alarm information.

FINISH TAB to check pending changes:

- Check the pending settings on each line by scrolling them on the screen.
  - If an alert is active, check each alert to ensure that the update can continue. If necessary, return to the corresponding screens and make the necessary changes.
  - If no alert is active, go to the <pump update> selection.
- To update the pump:
  - Touch the <update> button. The <confirm changes> dialog box will open.
    - If the changes are incorrect, touch the <cancel> button to return to the <finish> screen.
    - If the changes are correct, press the acknowledgement checkbox: "I have read and acknowledged all changes to the therapy and all pending alerts".





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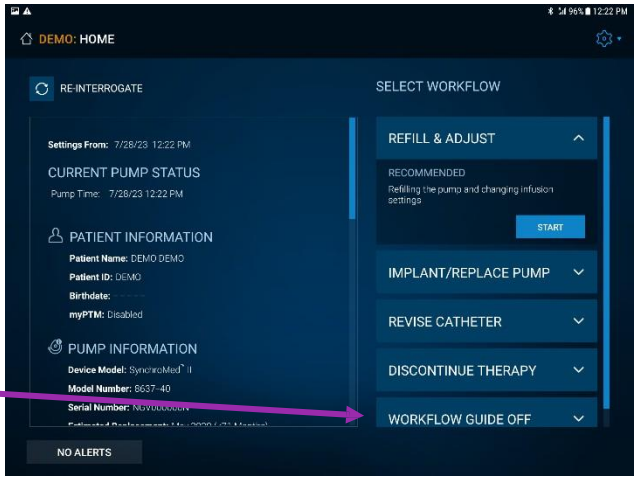
- Place the communicator on the implantable pump and press the <confirm> button. Telemetry begins and a progress window opens. Leave the communicator in place until the update is complete.



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<DISCONTINUE THERAPY> SCREEN

- Prevents a pump from delivering therapy temporarily or permanently.
- To set a minimum flow rate:
  - Select <minimum flow>. The dose per 24 h indicates the flow rate of 0.006 ml/day.
  - On the <finish> screen, update the pump.

END SESSION

- Once the update is complete, the application returns to the home screen, displaying information on the new programming.
- Touch the <settings> button in the action bar and select <end session>.
- Touch the <end session> button in the pop-up message.

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REPORT

1. Touch the <settings> button and select <reports>.
2. Touch the <download> button.
3. Connect the tablet to a computer.
4. On the tablet, select <authorize this device>. A window will open on the computer.
5. Select <open the device>.
6. Open <tablet>.
7. Open <reports> folder.
8. Save the PDF generated on the desktop, print it, and check it.
9. You can integrate the PDF into the patient's computerized records for programming traceability.

Update pump information on myPTM.

('resynchronize') with verification of next refill date.

TRACEABILITY AND DISCHARGE

(Physician + nurse)

- Computerized prescription validation
- VAS
- Refill IDDS
- Treatment
- Program next refill.
- Hospitalization report. Liaison letter given to patient with prescription.

III.4 PATIENT DISCHARGE

DRAFTING OF THE HOSPITALIZATION REPORT, with:

- Patient pain assessment, quality of life, autonomy, psychological state, modification of oral treatment,
- Number of activations (boluses performed) since last filling,
- Battery life (remember to arrange for replacement if <3 months),
- Efficacy,
- Tolerance,
- Any programming change,
- Date of next scheduled filling.

COMMUNICATION OF NEXT SCHEDULED FILLING TO PAIN NURSES

PROGRAMMING A WEEKLY CALL

For monitoring of efficacy and tolerance, and precise scheduling of next refill.

DAY HOSPITAL PLANNING IN CONJUNCTION WITH MANAGEMENT

END-OF-LIFE SITUATIONS

- Adaptability for home refilling or relay with local team / Hospital at Home

If the patient cannot be transported and bedside refilling is impossible => relay MORPHINE IV.

- Warn that the pump alarm will sound when it is empty.
  - If <1 mg IT of MORPHINE => 50 mg IV/24 h with free boluses,
  - If >1 mg IT of MORPHINE => 100 mg IV/24 h with free boluses.
- To be adapted to the patient's pain and clinical picture,
- Remember to remove the pump in the event of death. Dispose of battery in specific waste circuit (see Worksheet V.10).

IV.1 COMPLICATIONS / ADVERSE EVENTS LINKED TO THE INTRATHECAL TECHNIQUE

NB: "Most of these events are due to human error (programming errors, drug mixture preparation errors, etc.)."

INTRA- AND IMMEDIATE POST-OPERATIVE COMPLICATIONS

Technical and surgical

- Difficulties of approach, catheter positioning, failure,
- Hematoma of the pocket,
- Meningeal bleeding,
- Spinal cord compression by hematoma,
- Radiculalgia (positioning of catheter),
- Spinal cord or nerve injury.

Infectious

- Meningitis,
- Local cutaneous and subcutaneous, tunnelitis.

EARLY COMPLICATIONS (<15 DAYS)

CSF leakage

- Post-LP headache,
- Fluid collection either in the lumbar region or in the pocket: see Worksheet V.4,
- Failure to heal, with risk of exposure of implant: see Worksheet V.5.

LATE COMPLICATIONS

Implant-related

- Shifting of pump (cachexia, pocket too large),
- Shifting of catheter, disconnection, obstruction, kinks, folds, severing of catheter,
- Pump failures (rare event; if in doubt, contact the manufacturer).

Drug-related: see Worksheet IV.2

- Spinal mass syndrome associated with inflammatory granuloma: rapid loss of efficacy; possible spinal cord compression syndrome (high morphine concentration at low flow rates, rare in oncological situations),
- Morphine-related disorders,
- Ziconotide-related psychiatric disorders,
- Neurological disorders related to local anesthetics: motor weakness, paresthesia.

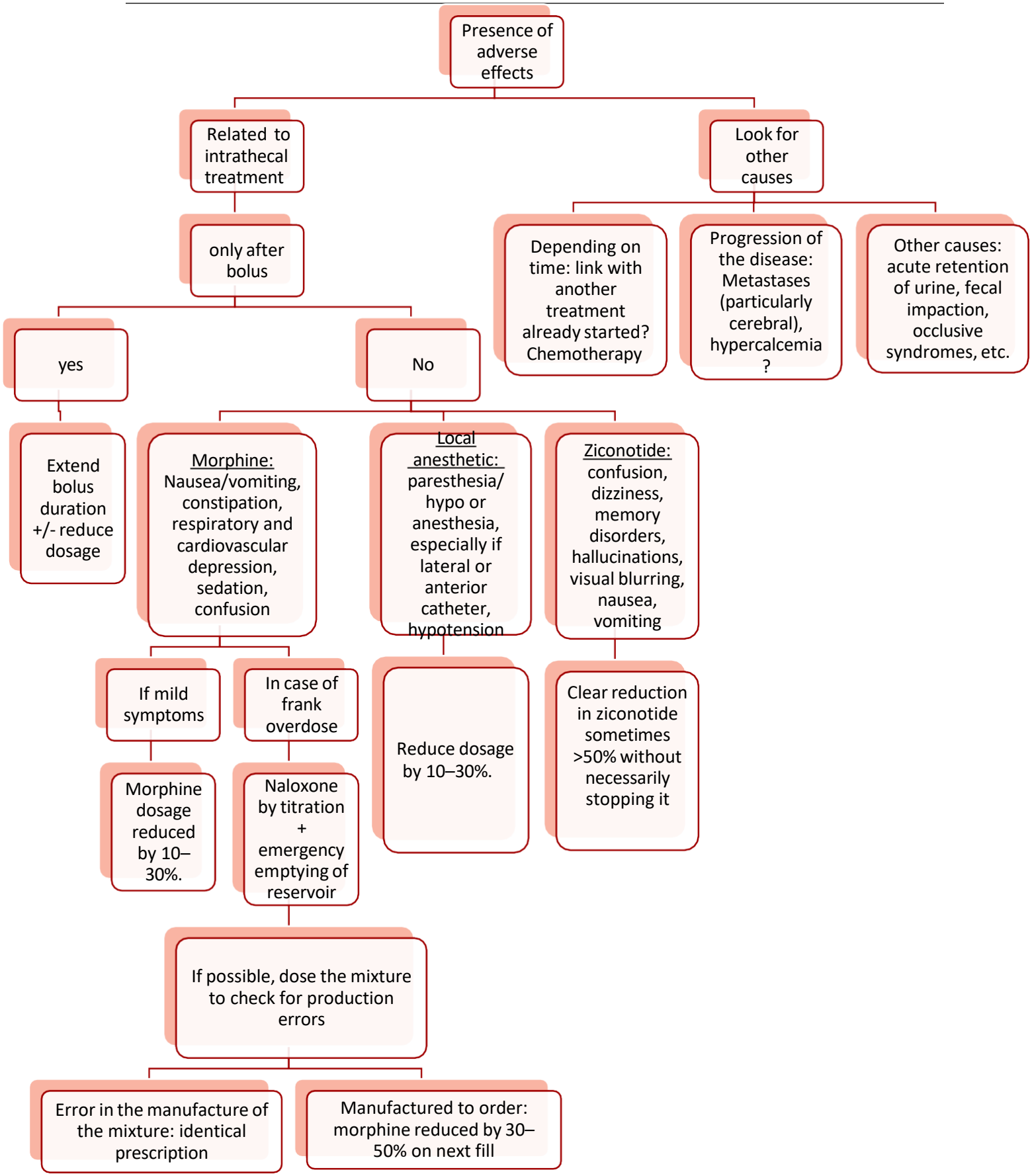
Filling-related: see Worksheet III.3

- Problem linked to approach: wrong needle location (if necessary, use long needle) SC injection (follow appropriate protocol, training +++),
- Infection, imperfect asepsis,
- Error in preparing intrathecal mixture,
- Non-use of specific equipment: Medtronic® refill kit 8551.

Programming-related: see Worksheet III.3

- Plan for pump battery replacement (battery status displayed during programming = battery life left in months),
- Programming error.

V.2 What to do about treatment-related adverse events



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V.1 EXPLANATORY WORKSHEET DESCRIBING THE INTRATHECAL ANALGESIA TECHNIQUE FOR CARE TEAMS

RATIONALE

- Obtain powerful analgesia by administering analgesic drugs into the cerebrospinal fluid.

PRINCIPLE

- Delivery of these analgesic drugs (opioids, local anesthetics, ziconotide) as near as possible to the receptors involved in the nociceptive message in the posterior horn of the spinal cord via an implanted catheter.

ADVANTAGES OF THE TECHNIQUE

- Relief of refractory pain unresponsive to conventional therapies,
- Reduced adverse effects,
- Improved quality of life,
- Preserved patient autonomy with a programmable implanted pump system, enabling intrathecal delivery of drugs contained in a reservoir, filled percutaneously and intermittently, according to the patient's drug consumption.

INDICATIONS (WORKSHEET I.4)

- Analgesic technique proposed for localized and/or regional pain, most often due to cancer, insufficiently controlled by conventional analgesics or when such analgesics produce marked adverse effects.

- **Pain**: nociceptive, neuropathic or mixed (the most common in oncology) whether somatic or visceral:
  - Localized in an anatomical region (see Worksheet II.2),
  - Insufficiently relieved by systemic analgesics, or
  - Marked adverse effects.

CONTRAINDICATIONS

- Hindered CSF flow, intracranial hypertension (ICHT), active infection, uncorrected hemostasis disorders (Worksheet I.4).

ORGANIZATION

- Collegial validation of the indication,
- Joint approach with oncology team and specific treatment,
- Explanation and information for the patient (Worksheet I.5), patient consent obtained.

MEANS

- Intrathecal placement of a catheter at the medial level of the metamers affected by the pain (it is important to place the catheter at the right metameric level and behind the posterior horn of the medulla),
- Implantation of a 40 ml (or 20 ml) subcutaneous pump connected to the catheter: continuous flow +/- boluses ,
- Need for a trained multidisciplinary team to monitor and guide patients (Worksheet I.1),
- Organization of the care pathway with GP/hospital relays.

ORGANIZATION OF PATHWAY (FITTING, FILLING, COORDINATING WITH ONCOLOGICAL TREATMENT) (WORKSHEET II.1.A).

Fitting

- Anesthesia team or interventional radiologist or neurosurgeon. Under GA (Worksheet II.2).

Safe prescription of drug mixture

- Using a calculator (Worksheet II.1.b).

Products

- Morphine +/- local anesthetic +/- ziconotide (neuropathic pain) (Worksheet I.3).

Induction

- In specialized departments, with dosage adjustment. We recommend stopping systemic opioid treatments (Worksheet II.3).

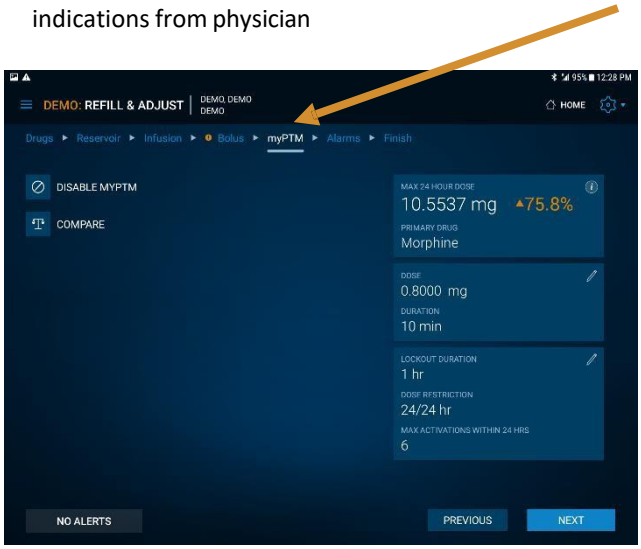
Maintenance

- Assessment (analgesic efficacy, tolerance) by pain team, date of next refill (Worksheet III.2.a),
- Prescription of mixture (one, two or three drugs) (Worksheet III.2.b),
- Transfer to pharmacist for preparation of syringe in ISO 5 cleanroom,
- Percutaneous pump filling by trained team, programmed according to prescription (Worksheet III.3).

On-call telephone service for emergencies, 7 days a week

V.2 BOLUS NOMENCLATURE WORKSHEET

Differentiate between boluses taken by the patient (myPTM - SynchroMed II pump) and boluses given on medical indications from physician



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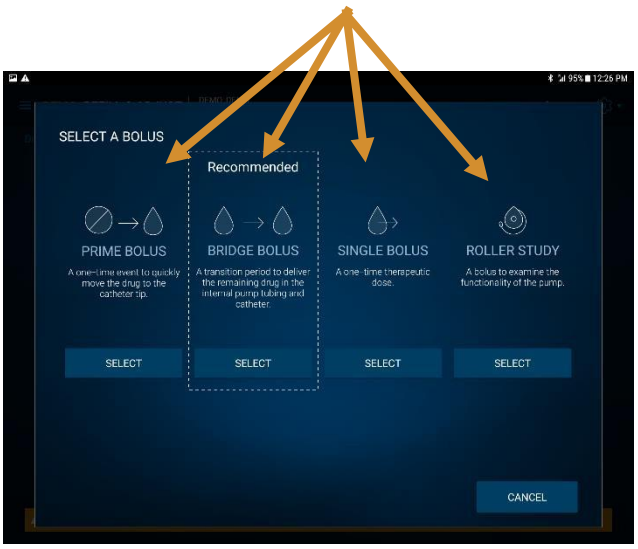

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PRIME BOLUS

Use:

- **At induction** after implantation (depends on the length of the implanted catheter entered by the implanter (data available by querying the pump or the operating report),
- When the pump is **restarted** after CSF sampling at set site,
- After **opacification of the catheter,**
- If the **pump is changed**.

BRIDGE BOLUS

- The bridge bolus is designed to completely purge the system during dosage changes. For technical reasons to do with fluid hydraulics, especially if we want to be sure that the system is completely purged, purging must be very slow, sometimes 6 to 10 hours, during which time no myPTM bolus can be administered.
- In simple terms, given the flow rates used for intrathecal analgesia in cancer patients, the bridge bolus is pointless, as the catheter is purged (0.2 ml max) within a few hours sometimes with a single bolus. It can therefore be ignored.
- The bridge bolus is useful only for patients on Lioresal (baclofen), who have very high flow rates and concentrations, with life-threatening risks on abrupt withdrawal.

SINGLE BOLUS OR PHYSICIAN BOLUS

- Purge the catheter for the same length of time as the patient's myPTM bolus. Only if doses are increased.
- Other clinical situations:
  - After the IDDS has been programmed during a filling operation because the patient is blocked during the specified refractory period.
  - Hyperalgesic patients in the refractory period or who have used up all their boluses. Dosage and duration determined by the prescribing physician.

ROLLER STUDY

- For checking pump operation (see Worksheet V.6).

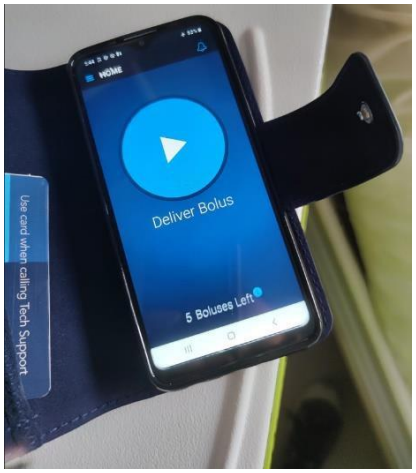
V.3 HOW TO USE THE MYPTM REMOTE CONTROL

= MYPTM on the Medtronic® pump

Dedicated smartphone plus communicator required.

1°) Switch on the smartphone. Touch the **myPTM** icon.

- This either indicates <u>that a **bolus is possible** or else gives the **time remaining** before a new bolus can be administered.</u>



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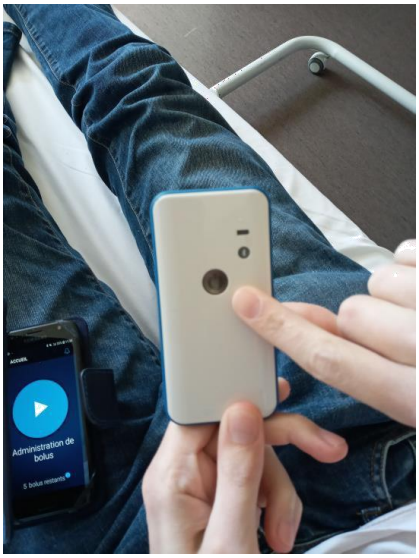

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2°) Switch on the communicator

- The top-right indicator light flashes.

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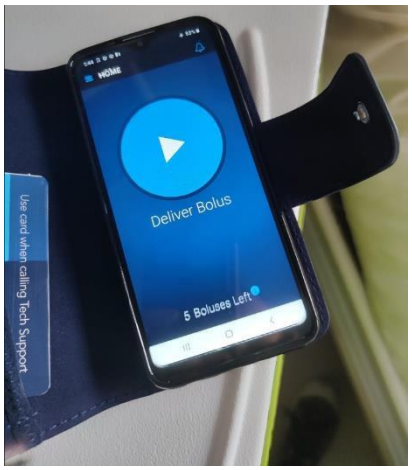
3°) On the smartphone touch <**Deliver Bolus**>



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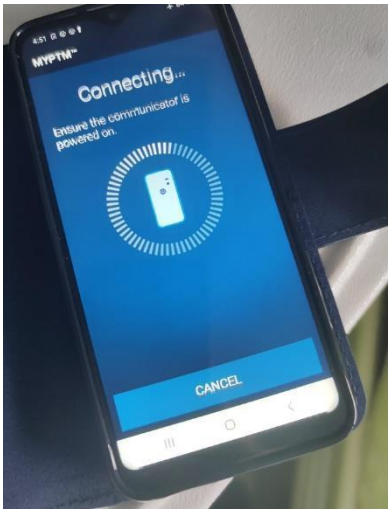
- Then place the activated communicator (blue light on) next to the pump and start the procedure.



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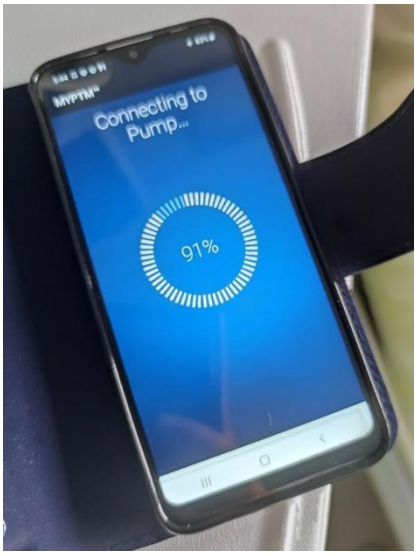
- The smartphone indicates whether communication with the pump has been established.



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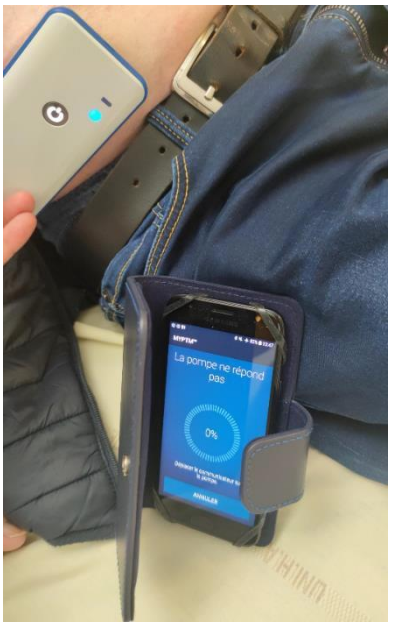
- In this situation of no communication with the pump, place the communicator once more next to the pump.



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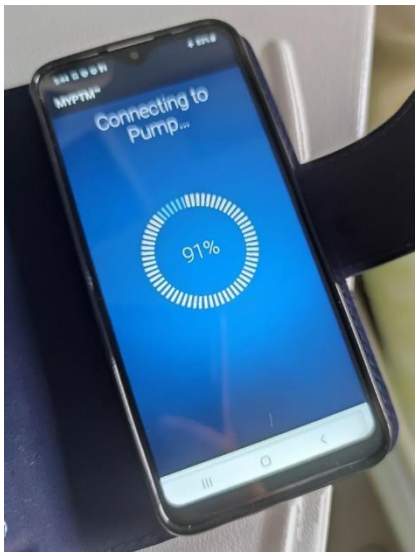

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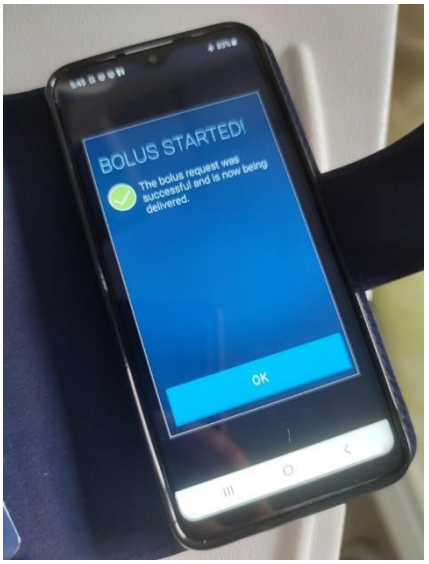
- When 100% is reached, the bolus will be activated according to the programmed settings.



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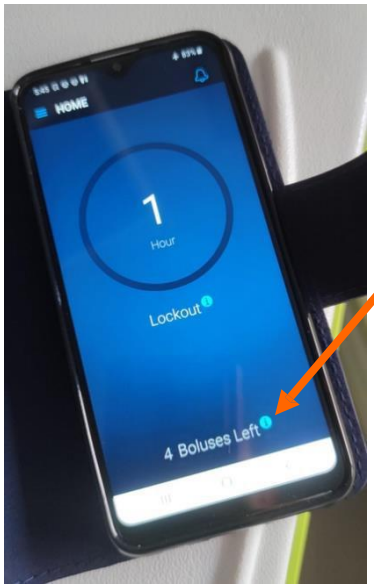
- Once the bolus request has been recorded, the refractory period is displayed. To get treatment details, touch <i>.



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What to do if a collection appears after an intrathecal pump has been implanted

SIGNS OF INFECTION?
- fever
- local inflammatory signs
- meningism
+/- hyperleukocytosis and raised CRP

DEHISCENCE?
Whatever the location, recontact the implantologist for possible redo (probable underlying infection)

NO

Presence of a discharge?

YES

Take sample and culture systematically

Either purulent fluid: cf. infection

Or clear fluid : urine test strip + for glucose points to CSF

NO

Location of the collection

Site of pump implantation
(most often abdominal)

Time when the collection appeared

Immediately post-operatively (3 weeks)

Collection in **small quantity** (does not hinder pump filling):
- Either CSF (beware migration of catheter): imaging (X-ray or CT scan)
- Or blood/serum

What to do:
Simple monitoring

If sudden loss of antalgia, check for disconnection of catheter.
-> ultrasound exploration or 3D CT scan

Collection **in large quantity** (hinders filling - ballottement): probable inflammatory liquid

What to do:
- Simple monitoring
- Compression dressings
- Drainage (under ultrasound) to be avoided if possible, but sometimes unavoidable (ballottement too great)
- Discuss repositioning the pump (less deep)

Collection appeared **some time** after implantation

1. Disconnection of catheter (ultrasound, 3D CT scan)
2. Suspected infection: monitor for signs of infection
3. Inflammatory fluid (cf. collection in large quantity)

Lumbar scar

Most often dura mater breach with CSF leakage

Spontaneous resorption in 4-6 weeks (longer if patient has a chronic cough)

What to do:
1. Simple monitoring; compression/elastic dressing, favor decubitus
2. X-ray or CT scan to check lumbar positioning of catheter (subcutaneous tunneling?)
3. Ask for implantologist's opinion
4. If post-LP syndrome: discuss peridural blood patch, with drainage at end of scar (less risk of infection and puncture of catheter) - cf. "immediate post-op" worksheet

YES
(whether or not there is a discharge, and whether or not the discharge occurred soon after implantation)

If vital prognosis linked to cancer not poor in short term:
- Removal of hardware
- Sampling

Resumption of analgesics by general route- cf. Worksheet III4

If vital prognosis linked to cancer poor in short term (weeks):
- Sampling of discharge for analysis and culture
- Then long-term antibiotic therapy and maintenance of intrathecal therapy (benefit/risk ratio in favor of maintaining intrathecal analgesia)

V.5 AFTER IMPLANTATION: POOR HEALING: WHAT SHOULD BE DONE?

SEARCH FOR CAUSES

Compliance with timeframes for stopping and restarting chemotherapy/anti-angiogenic drugs/other drugs, etc. after implantation?

- Avoid corticosteroids and NSAIDs.
- Contact with oncologist. Resumption too rapid? Cessation ill-planned? (caution with oral therapies: check patient's understanding):
  Reminder:
  - **Chemotherapy**: stop at least 15 days before the procedure and resume 7–10 days later if healing is good,
  - **Immunotherapy**: no foreseeable complications related to the procedure,
  - **Tyrosine kinase inhibitors**: no foreseeable complication related to the procedure except those with anti-angiogenic action (axitinib, sunitinib, pazopanib, regorafenib, lenvatinib), see below,
  - **Anti-angiogenic agents**: bevacizumab: stop at least three weeks before implantation and restart 15 days to three weeks later, provided healing is good.

Nutritional status?

- Nutritional assessment, dietician's advice if necessary.

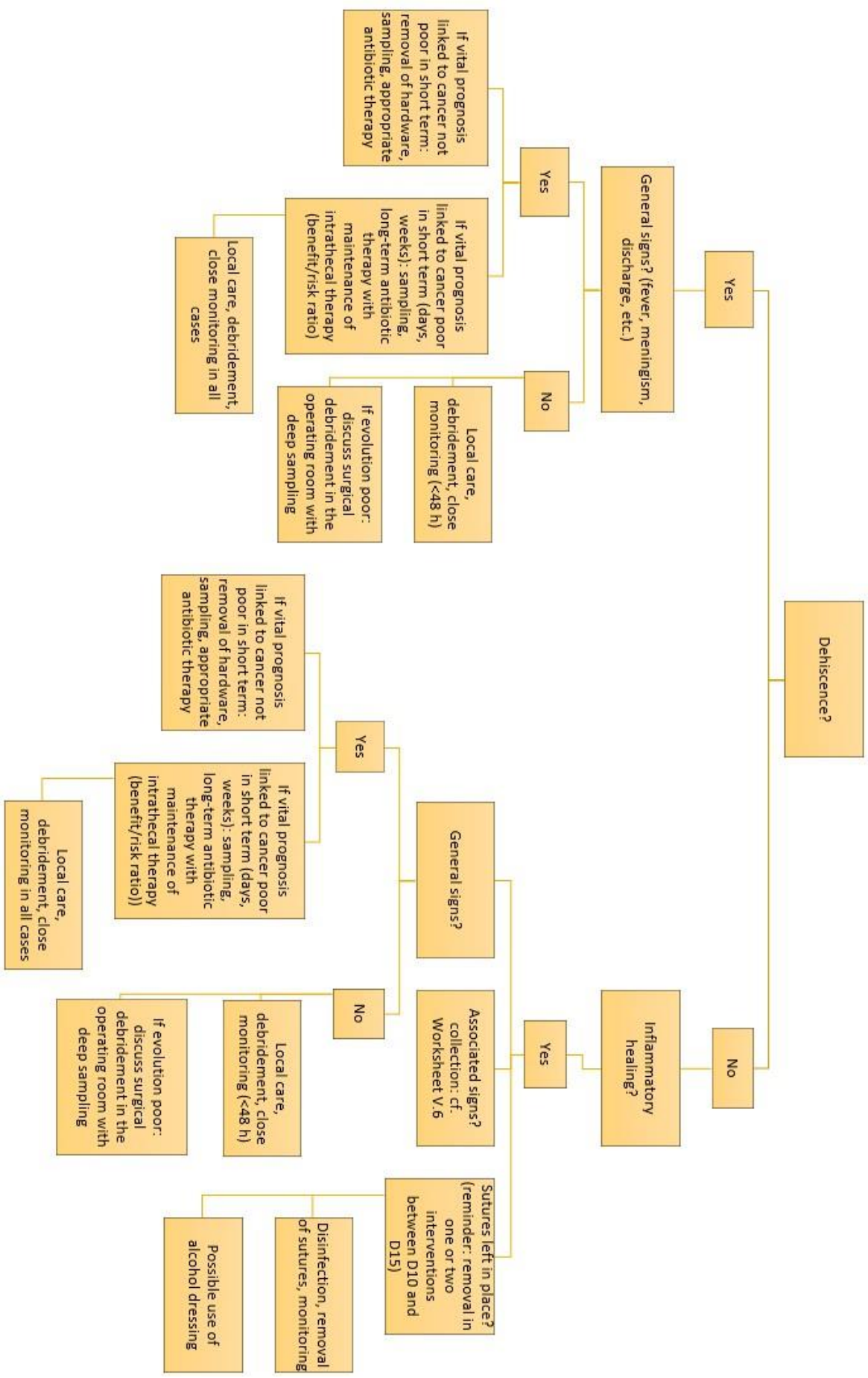
Skin condition?

- Irradiated zone?

SPECIFIC CARE

- If the implant does not heal properly, the implantologist must be contacted again, but this does not necessarily mean that the implant will have to be removed.
- Close monitoring of care in all cases, if care is provided at home, with regular consultations at the referring hospital.

V.5 The IDDS in practice: what to do about poor healing



V.6 PATIENT FITTED WITH AN IDDS AND ONSET OF ACUTE PAIN

I. KNOW THE LEVEL OF THE CATHETER (DATA GIVEN IN THE OPERATING REPORT)

II. SPECIFY WHETHER:

- Pain present in analgesic zone covered by IT catheter, or
- Pain outside the area covered by IT catheter.

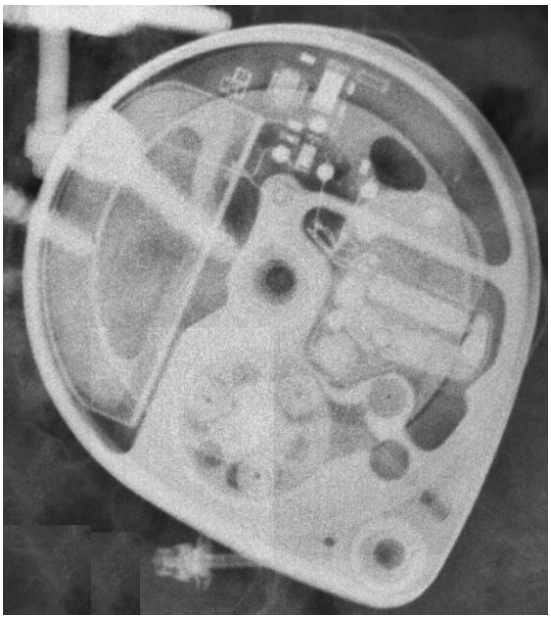
A. If pain in analgesic zone covered by IT catheter

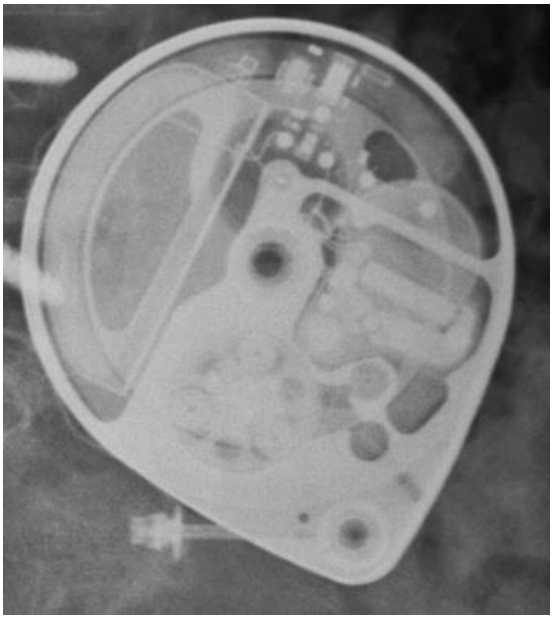
- Has an alarm been triggered?

YES: check critical alarm: empty tank, end of rated pump life, motor stalled, or 48-hour shutdown (see Worksheet V.9).

NO: equipment check by simple CT scan + /- catheter opacification:

- Disconnected or displaced catheter (see Worksheet IV.1),
- If scan shows no technical anomaly, investigate etiology of pain change and re-evaluate IT dosage (see Worksheet III.2.b). Pump failure without alarm is extremely rare,
- Possibly perform two unprepared abdominal examinations from the front: rotor examination (different positions of the pump rollers, indicating that the pump is working properly).





B. Pain outside the analgesic zone covered by the IT catheter

- Depending on the context:
  - *Make etiological diagnosis.*
  - MRI possible if pump checked after examination (see Worksheet V.7),
  - Local analgesic treatment possible: radiotherapy, interventional radiology, etc.,
  - Localized treatment impossible or pending specific treatment: analgesics [all possible drugs or routes of administration (if SC, distant from intrathecal pump, no injection at abdominal level). Avoid delayed-release forms or continuous flow and/or co-analgesics. Reinforce monitoring if opioids are used.

- NB: Inform the patient's IT referral team, especially if using strong opioids,

- Do not stop the intrathecal pump without advice from the referral team.

V.7 WHAT TO DO TO CARRY OUT MRI ON A PATIENT FITTED WITH AN IDDS

MRI-compatible pump up to 3 T.

PRECAUTION

MRI must be performed in a center where the pump can be re-queried at the end of the examination or, at the very least, a follow-up consultation organized in a suitable center 30 minutes after the examination.

BEFORE THE EXAMINATION

- **Tell the radiologist that a pump is fitted and that it is compatible with the examination, and that the pump must be queried by a specialized team afterwards.**

DO NOT STOP THE PUMP BEFORE THE EXAMINATION

DURING MRI

The magnetic field will disable the pump by stopping its rotor.

- If MRI time exceeds 20 min, an audible alarm is triggered. The examination must not be interrupted.
- In principle, normal operation is resumed after the examination is finished, but

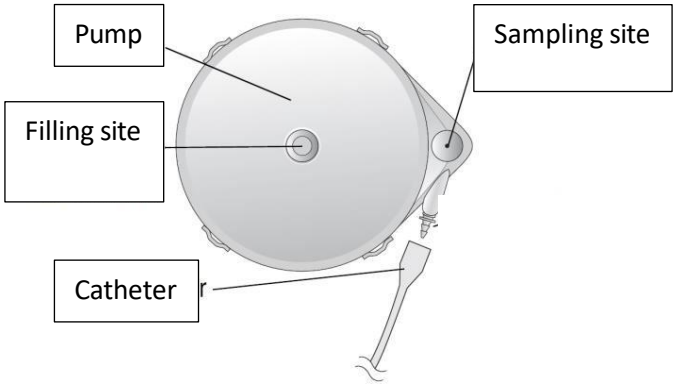
AFTER MRI the pump must be <u>systematically queried (20 min later)</u> to make sure it has restarted.

Rotor stoppage during examination is recorded in the event log, along with the restart check 20 min after the magnetic field has been removed.

- If the pump has not restarted: reprogram it.

V.8 PROCEDURE FOR SAMPLING CSF FROM PUMP

On SynchroMed II pumps, there is a **filling site** and an independent CSF **sampling site** (do not perform a "conventional" lumbar puncture - risk of catheter damage).



Hardware

- Template to be placed over the pump to locate the site,
- Specific access kit (Ref 8540): 10 ml syringe, extension tubing fitted with clamp, 25G needle.

PROCEDURE

Do not stop the pump.

- Surgical asepsis++, gowning, sterile gloves, fenestrated drape.
- Connect needle plus clamped connector to 10 ml Luer Lock syringe.
- Puncture site using the template.
- Feel the needle make contact with the metal back.
- Declamp.
- Aspirate 2 ml to purge catheter of mixture, reclamp, empty syringe.
- Change syringe, declamp.
- Sample CSF.
- Reclamp.
- Withdraw.

Then

- Initiate a “single physician bolus” (See Worksheet V.2) to fill the catheter with the mixture.

V.9 WHAT TO DO IF AN IDDS ALARM SOUNDS

The pump sounds an alarm to signal certain events.

The alarm sounds can be heard when settings are made.

Query the pump to find out the reason for the alarm.

There are critical and non-critical alarms.

CRITICAL ALARM

➔Signals that the treatment is jeopardized.

A critical alarm has two 3-second tones emitted by the pump when one of the following conditions occurs (value can be set during programming: 10 min increments to 2 h):

- Reservoir empty – estimated volume of reservoir is 0 ml,
- End of rated pump life,
- Stalled motor – the pump has detected that the motor has stalled,
- Prolonged shutdown – pump stopped for more than 48 hours.

NON-CRITICAL ALARM

➔Requires the attention of a physician but does not mean the treatment is jeopardized.

A non-critical alarm is an alarm with one 3-second tone emitted by the pump when one of the following conditions occurs: (value can be set during programming: 1 h increments to 6 h)

- Reservoir almost empty – the estimated tank volume is below the tank alarm volume (default setting 2 ml),
- Pump replacement time (PRT) – dated alarm based on the rated life of the implanted pump, indicating 90 days to end of rated life.

V.10 MANAGEMENT OF IDDS-FITTED PATIENTS AT END-OF-LIFE

- Maximum planning for end-of-life at home or non-transportable patient,
- If transport is iterative and very restricting, a change of equipment may be considered: externalize the catheter or intrathecal site and insert a PCA in hospital to have a larger reservoir.

Link with home caregivers important (GP/ nurses/ network / Hospital at Home)

IF POSSIBLE

Fill the pump at the patient's home (see Worksheet III.3) and program the pump.

IF IMPOSSIBLE TO FILL THE PUMP AT HOME

=> MORPHINE IV relay

- Set pump to minimum flow.
- Warn that the pump alarm will sound when it is empty.
- If <1 mg MORPHINE IT => 50 mg IV/24 h with free boluses between 1/10 and 1/24 of the daily dose, PR 15 to 30 minutes (no dose limit over 4 h),
- If >1 mg MORPHINE IT => 100 mg IV/ 24 h with free boluses between 1/10 and 1/24 of the daily dose, PR 15 to 30 minutes (no dose limit over 4 h),
- Adapt according to the patient's pain and clinical picture.

Remember to remove the pump after death. Waste disposal as for battery.

V.11 INTRATHECAL (IT) ANALGESIA WITH EXTERNAL PUMP

- IT analgesia with implanted pump is the reference method and should be offered if the conditions for its application are met (see Worksheet I.4).

- For patients with intractable regional pain, progressive disease and a short-term prognosis, implanted pumps are not suitable. Fitting requires general anesthesia, which is not always possible, and a preparation time incompatible with the need for rapid relief. Situations of opiate intolerance and acute trauma (e.g., femoral neck fracture refused for surgery, etc.) making the patient bedridden should also be considered.
  ➔ In such cases, intrathecal analgesia on an external pump should be discussed.

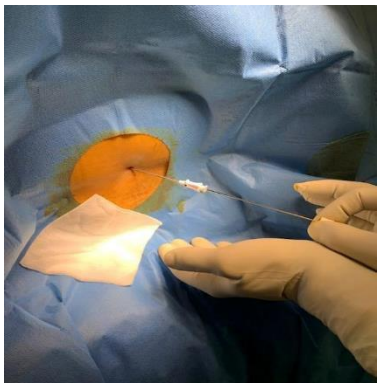
- Analgesia with an external pump affords patients an effective form of analgesia, despite a general condition that is often poor.

NECESSARY CONDITION

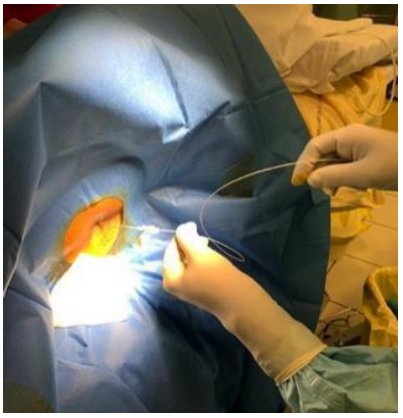
- Patient can remain in a comfortable lateral decubitus position,
- Other contraindications are set out in Worksheet I.4.

TECHNICAL ASPECTS

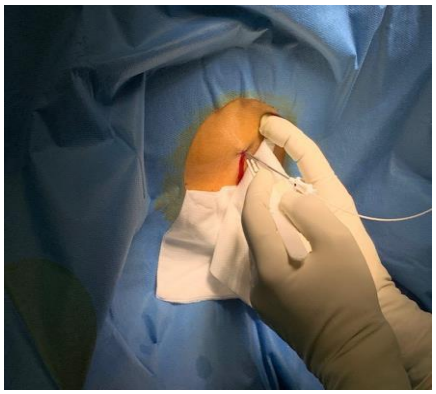
- Lateral decubitus position. Antibiotic prophylaxis. Electroscopic monitoring, BP, SaO2. Depending on context, oxygen therapy.



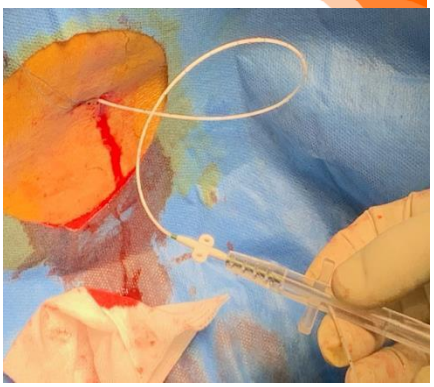
After surgical asepsis, patient draping and sterile dressing of the scope, a local cutaneous and subcutaneous anesthetic is administered prior to lumbar puncture at L3-L4 or L4-L5, i.e., below the terminal cone (located at T12/L1) (located at T12/L1).

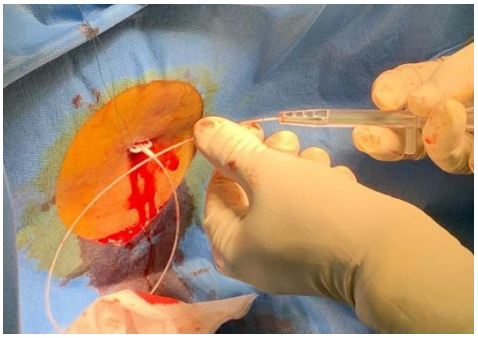


A 4-layer compression-resistant catheter is installed in the spinal canal under scopic monitoring, to place the catheter posteriorly at the spinal level corresponding to the targeted metamers (Worksheet II.2)



- A lumbar incision is then made around the Tuohy needle in place to create a pocket for placement of the fin crimped onto the catheter with the appropriate device and secured in depth with non-absorbable thread.





- The catheter is then tunneled using a Desilet tube after local subcutaneous anesthesia. The catheter is then brought out on the skin. Depending on the length implanted in the canal, a downstream segment can be added. The two segments are joined with a suitable connection system.

- At this stage, two technical options are possible:
  - Either insertion of a subcutaneous implantable chamber, which will then require an infusion device via a percutaneous Huber needle – patient on a hard flat surface, in a low thoracic position, or
  - Externalization of the catheter with direct connection to PCA-type pump tubing, via a secure connector fitted with an antibacterial filter.

- In both cases, suitable equipment is required: a reliable connection for an external catheter or a subcutaneous chamber.
- The lumbar wound and/or pocket is closed with a subcutaneous closing stitch and surface stitches, or an overlock.
- A biological sealant applied around the lumbar emergence of the catheter can be used to reduce CSF leakage and resulting headache.
- The catheter is then connected to a PCA-type pump (color-coded yellow: pump + tubing) for the perimedullary route.

MAKING UP THE INFUSION CASSETTE OR BAG

- As a first step, we advise having the hospital pharmacy make up a 100 ml bag/cassette, as described in Worksheet I.2, to facilitate the dosage adjustment phase. Depending on the context, the mixture will comprise morphine plus ropivacaine, with or without ziconotide.
- Initial dosages are adapted according to the patient's systemic treatment. Prescribing will use an adapted secure calculator.
- The pump will be set with flow rates in ml.

Note that the pump is accurate to within 0.1 ml, so flow rate values cannot be set finer than 0.1 ml. To facilitate initial dose modifications, we suggest initially setting the pump to a continuous flow rate of 0.2 ml/h, i.e., 4.8 ml/24 h, with 0.3 ml boluses (usually 12 boluses authorized over 24 h, with a minimum refractory period of 60 minutes).
➔This way, the dose can be decreased or increased according to the result obtained, without having to make up a fresh bag. Once equilibration has been achieved, a 250 ml bag is made up. Ideally, however, it should be renewed every three weeks to ensure the mixture remains stable.

MAINTENANCE AND MONITORING

- Wherever the patient is living, the medical and paramedical teams in charge of the patient must be informed and trained in the technique, possibly with the help of written documents. They must be able to contact the implanting center by telephone at any time.
- Connecting dressings must be regularly monitored and are replaced only when necessary. A clean dressing should not be routinely changed.
- Dressings on implantable chambers should leave the puncture site visible, with short Huber needles preferred. These should be changed as seldom as possible (once every 3 weeks).

ASSESSMENT AND FILLING

- Regular assessment of the analgesic effect and adverse effects must be carried out in order to adapt doses.
- Filling must be planned through regular contact with the pain referral team in charge of the patient. For bag changes, once the prescription has been validated and the bag filled, either the patient is taken to the referral center, or the bag is sent to the appropriate department by an approved carrier. Bag filling/change in this situation is carried out in the same way as pump filling, in a sterile environment. However, the technique for puncturing an implantable chamber is not the same as for venipuncture (no return, no rinsing).

COMPLICATIONS (WORKSHEET IV.1)

- Complications are the same as for an implantable pump.
- With implanted chambers, there is a risk of disconnection of the Huber needle. It is important not to re-infuse with the same needle. Needle disconnection demands a return to the referral center, with all the filling procedures previously described.
- Infectious complications will be limited by a closed system with as few interventions as possible, and bags prepared under sterile conditions at the hospital pharmacy.

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