

# GUIDELINES ON PAIN MANAGEMENT IN UROLOGY

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## General principles of cancer pain management

The therapeutic strategy depends on the four goals of care:

1. Prolonging survival
2. Optimising comfort
3. Optimising function
4. Relieving pain.

**Table 1: Hierarchy of general principles of cancer pain management**

1.	Individualised treatment for each patient.
2.	Causal therapy to be preferred over symptomatic therapy.
3.	Local therapy to be preferred over systemic therapy.
4.	Systemic therapy with increasing invasiveness: World Health Organization (WHO) ladder.
5.	Compliance with palliative guidelines.
6.	Both psychological counselling and physical therapy from the very beginning.

**Systemic analgesic pharmacotherapy: the ‘analgesic ladder’**  
Analgesic pharmacotherapy is the mainstay of cancer pain

management. Although concurrent use of other interventions is valuable in many patients, and essential in some, analgesic drugs are needed in almost every case.

Analgesic drugs can be separated into three groups:

- non-opioid analgesics;
- opioid analgesics;
- adjuvant analgesics.

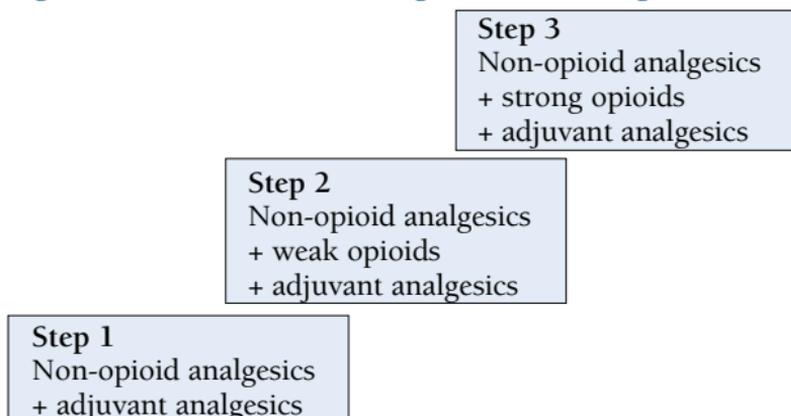
Adjuvant analgesics are drugs with other primary indications that can be effective analgesics in specific circumstances.

There are three groups:

- corticosteroids;
- neuroleptics;
- benzodiazepines.

The WHO has proposed a useful approach to drug selection for cancer pain, known as the ‘analgesic ladder’. When combined with appropriate dosing guidelines, this approach is capable of providing adequate relief to 70-90% of patients (Figure 1) (LE: 1a).

Figure 1: The World Health Organization's 'analgesic ladder'



**Table 2: Treatment of neuropathic pain**

Drug	Dosage	Frequency (maximum)
Amitriptyline (nortriptyline)	25-75 mg	Once per day
Gabapentin	600-1200 mg	Three times daily
Pregabalin	75-300 mg	Twice daily
Tramadol	50-100 mg	Four times daily

Recommendation	GR
Amitriptyline and nortriptyline are first-line treatment for neuropathic pain; nortriptyline has fewer side-effects.	A
Tricyclic antidepressants (TCA) must be used cautiously in patients with a history of cardiovascular disorders, glaucoma, and urine retention.	A

Gabapentin and pregabalin are first-line treatments for neuropathic pain, especially if TCAs are contraindicated.	A
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GR = grade of recommendation.

## Pain management in urological cancers

**Table 3: Docetaxel-based chemotherapy versus mitoxantrone-based regimens in prostate cancer**

Chemotherapy agent	Plus additional therapy	Frequency	Response rate	
			Pain (%)	QoL (%)
Docetaxel	Prednisone	Every 3 weeks	35	22
Docetaxel	Prednisone	Weekly	31	23
Mitoxantrone	Prednisone	Every 3 weeks	22	13

Recommendation: Anticancer treatment	LE	GR
Hormonal therapy (orchiectomy, LHRH analogues, diethylstilboestrol equivalent)	1a	A
Total androgen blockade: flare prevention, second line	2b	B
Intermittent androgen suppression: experimental	3	B
Monotherapy with anti-androgen: currently not recommended	1b	A

First-line treatment controls disease for 12-18 months; second line individualised	1b	A
<i>Supportive care</i>		
Low-dose glucocorticoids	1b	A
<i>Chemotherapy</i>		
Mitoxantrone plus prednisolone	1b	B
Estramustine + vinblastine or etoposide or paclitaxel	2b	B
Docetaxel	1b	A
<b>Pain management</b>		
Pain assessment (localisation, type, severity, overall distress)		B
<i>Pain due to painful and stable bone metastases (single lesions)</i>		
External beam irradiation	1b	A
<i>Pain due to painful bony metastases (widespread)</i>		
Primary hormonal therapy	1a	A
Radioisotopes (strontium-89 or samarium-153)	2	B
Bisphosphonates	1b	A
<i>Systemic pain management</i>		
World Health Organization analgesic ladder step 1: NSAID or paracetamol	1a	A
<i>Opioid administration</i>		
Dose titration	2	B
Access to breakthrough analgesia	1b	A
Tricyclic antidepressant and/or anticonvulsant in case of neuropathic pain	1a	A

NSAID = non-steroidal anti-inflammatory drug.

## External beam radiation

- Single-fraction radiotherapy is an excellent palliative treatment for symptomatic bone metastases, resulting in complete or partial pain relief in 20-50% and in 50-80% of patients, respectively.
- Metastatic epidural spinal cord compression is a severe complication requiring urgent treatment. Direct decompressive surgery is superior to radiotherapy alone. Primary radiotherapy is recommended for patients who are not suited for surgery.
- For impending pathological fractures, a prophylactic orthopaedic procedure should be considered.

**Table 4: Criteria for selecting patients for primary therapy for spinal cord compression**

Absolute criteria	Surgery	Radiotherapy
Operability	Medically operable	Medically inoperable
Duration of paraplegia	< 48 hours	≥ 48 hours
Life expectancy	≥ 3 months	< 3 months
Radiosensitivity		Highly sensitive
Relative criteria		
Diagnosis of primary tumour	Unknown	Known
Bone fragments with compression	Present	Absent
Number of foci of compression	1 focus	> 1 foci

## Radioisotopes

The most important radiopharmaceuticals are:

- $^{89}\text{Sr}$  (strontium-89 chloride);
- $^{153}\text{Sm}$  (samarium-153 leixidronam);
- and, to a lesser extent,  $^{186}\text{Re}$  (renium-186 etidronate).

There is no clear difference in treatment response between  $^{89}\text{Sr}$ ,  $^{153}\text{Sm}$  and  $^{186}\text{Re}$ . However, there is a difference in onset of response, duration of response and toxicity. For  $^{153}\text{Sm}$  and  $^{186}\text{Re}$ , the onset of response is rapid, but duration is shorter than  $^{89}\text{Sr}$ .

$^{89}\text{Sr}$  and  $^{153}\text{Sm}$  leixidronam are indicated for treatment of bone pain, resulting from skeletal metastases involving more than one site and associated with an osteoblastic response on bone scan but **without** spinal cord compression (LE: 2, GR: B). Overall, the response rate is 60-80%. However, pain reduction is unlikely to occur within the first week, and can occur as late as 1 month after injection. Analgesics should therefore continue to be prescribed to patients until bone pain improves.

If the pain responds to the initial treatment, administration of  $^{153}\text{Sm}$  leixidronam can be repeated at intervals of 8-12 weeks in the presence of recurrent pain (LE: 2, GR: B).

Radiopharmaceuticals should not be administered if the glomerular filtration rate is  $< 30$  mL/min in patients who are pregnant or who are breast feeding. Because of myelosuppression, a white blood cell count  $> 3500/\mu\text{L}$  and a platelet count  $> 100,000/\mu\text{L}$  are desirable.

## Post-operative pain management

Recommendations	GR
Post-operative pain should be treated adequately to avoid post-operative complications and the development of chronic pain.	B
Pre-operative assessment and preparation of the patient allow in more effective pain management.	A
Adequate post-operative pain assessment can lead to more effective pain control and fewer post-operative complications.	B

## Specific pain treatment during ESWL

**Table 5: Analgesic drug options during extra-corporeal shock wave lithotripsy (ESWL)**

Drug	Dosage	Method of administration	Frequency (maximum)
Alfentanil	0.5-1.0 mg/70 kg	Intravenously	On demand
Fentanyl (or sufentanil or remifentanyl)	1 µg/kg	Intravenously	On demand (risk of respiratory depression)

Recommendations	GR
Analgesics should be given on demand during and after ESWL because not all patients need pain relief.	B
Premedication with NSAIDs or midazolam often decreases the need for opioids during the procedure.	B
Intravenous opioids and sedation can be used in combination during ESWL; dosage is limited by respiratory depression.	C
Post-ESWL, analgesics with a spasmolytic effect are preferable.	C

ESWL = extracorporeal shock wave lithotripsy; NSAID = non-steroidal anti-inflammatory drug.

## Specific pain treatment after different urological operations

<b>Table 6: Analgesic drug options after transurethral procedures</b>			
Drug	Dosage (mg)	Method of administration	Frequency (maximum)
Diclofenac	50	Orally	Three times daily
	100	Rectally	Every 16 hours
Metamizole	500-1000	Orally or iv	Four times daily
Paracetamol	500-1000	Orally or iv	Four times daily
Tramadol	50-100	Orally, im, sc or iv	Four times daily

Piritramid	15	iv or sc	Four times daily
Pethidine	25-100	Orally, im, sc	Four to six times daily

*iv = intravenously; im = intramuscularly; sc = subcutaneously.*

Recommendations	GR
Post-operative analgesics with a spasmolytic effect or mild opioids are preferable.	C
Antimuscarinic drugs could be helpful in reducing discomfort resulting from the indwelling catheter.	B
Antimuscarinic drugs may reduce the need for opioids.	B

**Table 7: Analgesic drug options after laparoscopic surgery, minor surgery of the scrotum, penis, and inguinal region or transvaginal urological surgery**

Drug	Dosage (mg)	Method of administration	Frequency (maximum)
Metamizole	500-1000	Orally or iv	Four times daily
Paracetamol	500-1000	Orally or iv	Four times daily
Tramadol	50-100	Orally, im, sc or iv	Four times daily
Morphine	10	Intermittent im	Eight times daily
	1 mg bolus	iv	PCA, 5 minutes lockout

Diclofenac	50	Orally	Three times daily
	100	Rectally	Every 16 hours

*iv* = intravenously; *im* = intramuscularly; *sc* = subcutaneously;  
*PCA* = patient-controlled analgesia.

Recommendations	GR
Low intra-abdominal pressure and good desufflation at the end of the laparoscopic procedure reduces post-operative pain.	A
NSAIDs are often sufficient for post-operative pain control.	B
NSAIDs decrease the need for opioids.	B
For post-operative pain control after minor surgery of the scrotum, penis and inguinal region, multi-modal analgesia with a combination of NSAIDs or paracetamol plus local anaesthetics should be used.	B
If possible, avoid opioids for out-patients.	C
NSAIDs are often sufficiently effective after minor or moderate surgery.	B

*NSAID* = non-steroidal anti-inflammatory drug.

**Table 8: Analgesic drug options after major perineal open surgery, suprapubic extraperitoneal, retroperitoneal or transperitoneal laparotomy**

Drug	Dosage	Method of administration	Frequency (maximum)
Bupivacaine 0.25% + fentanyl 2 µg/mL	5-15 mL/hour	Continuous epidural infusion	Not applicable
Morphine	1 mg bolus	iv	PCA, 5-minute lockout
Metamizole	500-1000 mg	Orally or iv	Four times daily
Paracetamol	500-1000 mg	Orally or iv	Four times daily
Tramadol	50-100 mg	Orally, im, sc or iv	Four times daily
Piritramid	15 mg	iv or sc	Four times daily
	50 mg	Orally	Three times daily
	100 mg	Rectally	Every 16 hours

*iv = intravenously; im = intramuscularly; sc = subcutaneously; PCA = patient-controlled analgesia.*

Recommendations	GR
The most effective method for systemic administration of opioids is PCA, which improves patient satisfaction and decreases the risk of respiratory complications.	A
Epidural analgesia, especially PCEA, provides superior post-operative analgesia, reducing complications and improving patient satisfaction. It is therefore preferable to systemic techniques.	A

PCA = patient-controlled analgesia; PCEA = patient-controlled epidural analgesia.

## Analgesics

Recommendations	GR
Paracetamol can be very useful for post-operative pain management as it reduces the consumption of opioids.	B
Paracetamol can alleviate mild post-operative pain as a single therapy without major adverse effects.	B
NSAIDs are not sufficient as a sole analgesic agent after major surgery.	B
NSAIDs are often effective after minor or moderate surgery.	B
NSAIDs often decrease the need for opioids.	B
Avoid long-term use of COX inhibitors in patients with atherosclerotic cardiovascular disease.	B

NSAID = non-steroidal anti-inflammatory drug.

## Metamizole (dipyrone)

Metamizole is an effective antipyretic and analgesic drug used for mild-to-moderate post-operative pain and renal colic. Its use is prohibited in the USA and some European countries because of single reported cases of neutropenia and agranulo-cytosis. Dosage per day is 500-1000 mg four times daily (orally, intravenously or rectally). If given intravenously, metamizole should be administered as a drip (1 g in 100 mL normal saline).

**Table 9: Drug, administration, dosage and delivery**

Drug	Method of administration	Single dosage (mg)	Frequency	Maximal dosage (mg/24 hours)
<b>Antipyretics</b>				
Paracetamol	Orally	500-1000	Four times daily	4000 (50mg/kg)
	iv	1000	Four times daily	4000 (50mg/kg)
	Rectally	1000	Four times daily	4000 (50mg/kg)
Metamizole	Orally	500-1000	Four times daily	4000
	iv	1000	Four times daily	4000
<b>Conventional NSAIDs) (i.e. non-selective COX inhibitors)</b>				
Ketorolac	Orally or iv	10-30	Four times daily	40 orally 90 iv or im 60 iv or im (elderly)

Ibuprofen	Orally	200-800	Three times daily	2400
Ketoprofen	Orally or iv	50	Four times daily	200
Diclofenac	Orally or iv	75	Twice daily	150
	Orally or iv	50	Three times daily	150
	Rectally	100	Every 16 hours	150
<b>COX-2 selective inhibitors</b>				
Meloxicam	Orally	15	Once per day	15
Lornoxicam	Orally or iv	4	Three times daily	12
Celecoxib	Orally	100-200	Once per day	400
Parecoxib	iv form only	40	Once or twice daily	80
<b>Opioids</b>				
<i>Strong opioids</i>				
Morphine**	Orally or rectally	Starting with 10 mg	Six to eight times daily	No maximal dose
Morphine**	sc or im	Starting with 5 mg	Six to 12 times daily	No maximal dose
Morphine**	iv	Starting with 2 mg	Six to 12 times daily	No maximal dose

Pethidine (meperidine)	Orally, sc or im	25-150	Four times daily	500
Pethidine (meperidine)	Rectally	100	Four times daily	500
Pethidine (meperidine)	iv	25-100	Four times daily	500
Oxycodone	Orally, iv or sc	5-10	Four to six times daily	400
<i>Weak opioids</i>				
Tramadol	Orally iv	50 100	Four to six times daily	400-600
Codeine	Orally or rectally	30-60 (plus paracetamol)	Four times daily	300?

*\*\* A simple way of calculating the daily dosage of morphine for adults (20-75 years) is: 100 – patient’s age = morphine per day in mg.*

*NSAID = non-steroidal anti-inflammatory drug; sc = subcutaneous; im = intramuscularly; iv = intravenously.*

**Table 10: Common equi-analgesic dosages for parenteral and oral administration of opioids\***

Drug	Parenteral (mg)	Oral (mg)
Morphine	10	30
Fentanyl	0.1	–
Pethidine	75	300
Oxycodone	15	20-30
Dextropropoxyphene	–	50
Tramadol	37.5	150
Codeine	130	200

\*All listed opioid doses are equivalent to parenteral morphine 10 mg. The intrathecal opioid dose is 1/100th, and the epidural dose 1/10th, of the dose required systemically.

**Table 11: Typical patient-controlled analgesia (PCA) dosing schedule**

Drug (concentration)	Bolus size	Lockout interval (min)	Continuous infusion
Morphine (1 mg/mL)	0.5-2.5 mg	5-10	0.01-0.03 mg/kg/hour
Fentanyl (0.01 mg/mL)	10-20 µg	5-10	0.5-0.1 µg/kg/hour
Pethidine (10 mg/mL)	5-25 mg	5-10	–

Recommendation	GR
Intravenous PCA provides superior post-operative analgesia, improving patient satisfaction and decreasing the risk of respiratory complications.	A

**Table 12: Typical epidural dosing schemes\***

Drug	Single dose	Continuous infusion
Morphine	1-5 mg	0.1-1 mg/hour
Fentanyl	50-100 µg	25-100 µg/hour
Sufentanil	10-50 µg	10-20 µg/hour
Pethidine	10-30 mg	10-60 mg/hour
Bupivacaine 0.125% or ropivacaine 0.2% + fentanyl 2 µg/mL	10-15 mL	2-6 mL/hour

\* L-bupivacaine doses are equivalent to those of bupivacaine.

**Table 13: Typical patient-controlled epidural analgesia (PCEA) dosing schemes**

Drug	Demand dose	Lockout interval	Continuous rate
Morphine	100-200 µg	10-15	300-600 µg/hour
Fentanyl	10-15 µg	6	80-120 µg/hour
Pethidine	30 mg	30	–
Bupivacaine 0.125% + fentanyl 4 µg/mL	2 mL	10	4 mL/hour

Ropivacaine 0.2% + fentanyl 5 µg/mL	2 mL	20	5 mL/hour
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Recommendation	GR
Epidural analgesia, especially PCEA, provides superior post-operative analgesia, reducing complications and improving patient satisfaction. It is therefore preferable to systemic techniques.	A

**Table 14: Examples of neural blocks**

Procedure	Dosage	Drug
Iliohypogastric or ilioinguinal nerve infiltration after hernia repair	10-20 mL	Bupivacaine or ropivacaine 0.25-0.5%
Intercostal nerve infiltration	5-10 mL	Bupivacaine or ropivacaine 0.25-0.5%
Continuous intrapleural infusion	10 mL/h	Bupivacaine or ropivacaine 0.1-0.2%

Recommendations	GR
Multi-modal pain management should be employed whenever possible since it helps to increase efficacy while minimising adverse effects.	B
For post-operative pain control in out-patients, multi-modal analgesia with a combination of NSAIDs or paracetamol plus local anaesthetics should be used.	B

Multi-modal and epidural analgesia are preferable for post-operative pain management in elderly patients because these techniques are associated with fewer complications.	B
Post-operative use of opioids should be avoided in obese patients unless absolutely necessary.	B
An epidural of local anaesthetic in combination with NSAIDs or paracetamol is preferable in obese patients.	B
There are insufficient data to support a specific post-operative pain management plan for critically ill or cognitively impaired patients.	C

NSAID = non-steroidal anti-inflammatory drug.

## Peri-operative pain management in children

**Table 15: Pre-operative analgesia and sedation in children**

Drug	Dosage and route of administration	Action
Morphine sulfate	0.1 mg/kg	Can prevent crying, which therefore reduces oxygen consumption and pulmonary vasoconstriction
Atropine	0.01-0.02 mg/kg iv, im, orally, or rectally	Prevents bradycardia during induction of anaesthesia

Pentobarbital	4-6 mg/kg im	Pre-operative sedation and separation anxiety in children
Ketamine	6 mg/kg orally or intranasally	
Midazolam	0.5 mg/kg orally, intranasally, or rectally	
Dexmedetomidine	4 µg/kg orally or intranasally	
Clonidine	4µg/kg orally	
Chloral hydrate	50-100mg/kg orally	
Methoexital	25-30mg/kg rectally	
EMLA	Lidocaine 2.5%; prilocaine 2.5%	Local application decreases venepuncture pain

*iv = intravenously; im = intramuscularly.*

**Table 16: Post-operative analgesia in children**

Drug	Dosage	Administration	Severity of surgical procedure
Paracetamol	10-15 mg/kg every 4 hours	Orally, rectally	minor
	20-30 mg/kg every 6 hours		minor
Ibuprofen	10-15 mg/kg every 6 hours	Orally, iv, rectally	minor, medium

Naproxen	6-8 mg/kg every 8-12 hours	Orally, iv, rectally	minor, medium
Codeine	0.5-1 mg/kg every 3-4 hours	Orally	minor, medium
Morphine	0.1 mg/kg every 2-4 hours Infusion: 0.03 mg/kg/hour	0.3 mg/kg every 3-4 hours iv, sc Orally	medium, major
Oxycodone	0.1-0.2 mg/kg every 3-4h	Orally	medium
Hydromorphone	0.04-0.08 mg/kg every 3-4 hours	Orally	medium
Tramadol	1 mg/kg every 4-6 hours	iv	medium, major
Pethidine	2-3 mg/kg every 3-4 hours	iv	medium, major

*iv = intravenously; sc = subcutaneously.*

Patient-controlled analgesia can be used safely in children more than 6 years old. In infants and children unable to use PCA, nurse-controlled analgesia is effective. Locoregional techniques such as wound infiltration, nerve blocks, caudal and epidural analgesia are also used successfully.

## Non-traumatic acute flank pain

### Urological causes:

- Renal or ureteral stones
- Urinary tract infection (pyelonephritis, pyonephrosis, or renal abscess)
- Uretero-pelvic junction obstruction
- Renal vascular disorders (renal infarction, renal vein thrombosis)
- Papillary necrosis
- Intra- or peri-renal bleeding
- Testicular cord torsion

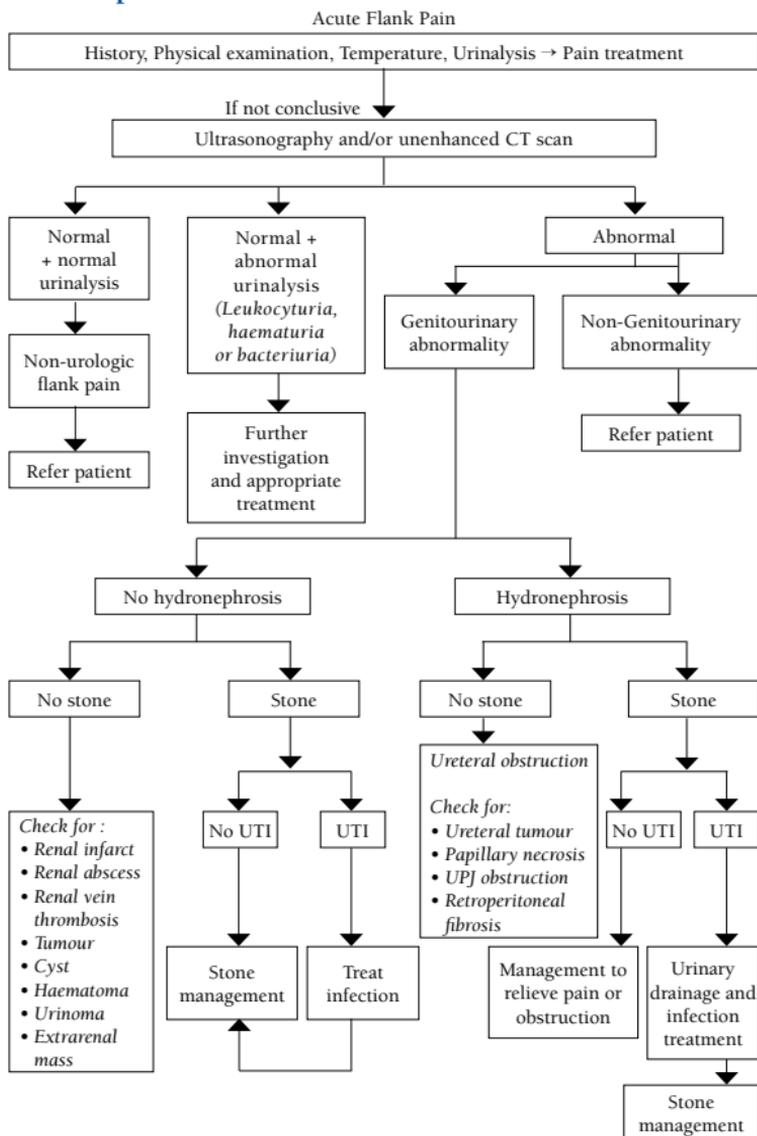
### Laboratory evaluation

All patients with acute flank pain require a urine test (red and white cells, bacteria or urine nitrite), blood cell count, and serum creatinine measurement. In addition, febrile patients require C-reactive protein (CRP) and urine culture. Pyelonephritis ± obstructive uropathy should be suspected when the white blood count exceeds 15,000/mm<sup>3</sup>.

### Diagnostic imaging

Recommendations	GR
Febrile patients ( $\geq 38^{\circ}\text{C}$ ) with acute flank pain and/or with a solitary kidney need urgent imaging.	B
Unenhanced helical CT (UHCT) is the imaging diagnostic modality with the highest sensitivity and specificity for evaluation of non-traumatic acute flank pain.	A
Ultrasound can be an alternative to UHCT in the initial approach to non-traumatic acute flank pain.	A

**Figure 2: Diagnostic approach to non-traumatic acute flank pain**



CT = computed tomography; UTI = urinary tract infection.

For a quick Differential Diagnosis and Management Options the Decision tree (figure 2) is suggested:

## Initial emergency treatment

### *Systemic analgesia*

Pain relief is usually the first, most urgent, therapeutic step:

- A a slow intravenous infusion of dipyrone, 1 g or 2 g, is just as effective as diclofenac (75mg bolus) (LE: 1a).
- Intravenous papaverine (120 mg) can effectively and safely relieve patients not responding to conventional agents (diclofenac) and can be an alternative to diclofenac in patients with contraindications to NSAIDS (LE: 1b).
- The combination of intravenous morphine + ketorolac seems superior to either drug alone and appears to be associated with a decrease in rescue analgesia.

Recommendation	GR
NSAIDs such as diclofenac (75 mg, bolus), and dipyrone (1-2 g, slow intravenous injection) are both very effective for acute flank pain.	A

### *Upper urinary tract decompression*

If pain relief cannot be achieved using medical therapy and there are signs of infection and of impaired renal function, upper urinary tract drainage should be carried out (Ureteral stenting or percutaneous nephrostomy).

## Indications for stenting for urgent relief of obstruction

- Urine infection with urinary tract obstruction
- Urosepsis
- Intractable pain and/or vomiting
- Obstruction of a solitary or transplanted kidney
- Bilateral obstructing stones
- Ureteral calculus obstruction in pregnancy

## Aetiological treatment

*Urolithiasis* should be treated as defined in the *EAU Guidelines on Urolithiasis*.

Infectious uncomplicated conditions (i.e. acute pyelonephritis in otherwise healthy individuals) should be treated with appropriate antibiotics and analgesics.

When a diagnosis of UPJ obstruction, papillary necrosis, renal infarction renal vein thrombosis, spontaneous renal hemorrhage or testicular cord torsion has been made the patient should be treated accordingly (*see long version*).

*This short booklet is based on the more comprehensive EAU guidelines (ISBN 978-90-79754-70-0), available to all members of the European Association of Urology at their website - <http://www.uroweb.org/guidelines/online-guidelines/>.*