

Targeted Drug Delivery

Key Points

- In all patients with persistent pain, appropriate evaluation requires assessment of the physical, psychological and socio-environmental factors, prior to selecting treatment options.
- Targeted Drug Delivery (TDD) therapy delivers pain medicine directly to the cerebral spinal fluid in the intrathecal space which is surrounding the spinal cord.
- TDD involves a pump connected to a thin, flexible catheter, placed beneath the skin.
- The ability to target drug delivery enables patients to experience pain relief with a small fraction of an oral medication dose.
- TDD can involve a screening test to assess effectiveness prior to implant, and is reversible.

What is Targeted Drug Delivery?

Targeted Drug Delivery (TDD), also known as intrathecal drug delivery, uses an implanted infusion system to manage severe chronic pain, including intractable cancer pain. An implanted pump releases pain-relieving medication through a thin, flexible catheter directly to the intrathecal space surrounding the spinal cord where pain signals travel, interrupting pain signals before they reach the brain.

The ability to target drug delivery enables patients to experience pain relief with a small fraction of an oral medication dose¹, which can help to minimise the uncomfortable and sometimes intolerable side effects (e.g. drowsiness, dizziness, dry mouth, nausea, vomiting and constipation) that often accompany pain medication taken orally.^{2,3,4,5,6,7}

More than 150,000 people have received TDD to treat chronic pain worldwide.⁸

Who is a suitable candidate for Targeted Drug Delivery?

TDD is indicated for patients with severe chronic pain. Consensus guidelines suggest a thorough, multi-faceted approach to the patient selection process for TDD. In general, TDD may be considered for patients who have:

- Chronic, intractable pain
- Not received adequate relief from more conservative treatments, including oral morphine-like drugs
- No untreated drug addiction
- No contraindications to implantation
- There is objective evidence of pathology concordant with the pain complaint
- Other surgical intervention is not indicated
- A psychological evaluation of the patient has been completed and clearance given

What does the procedure involve?

TDD can involve two stages for patients recommended for the therapy; a screening test, followed by the implant procedure. A *screening test* provides an opportunity to assess the effectiveness and potential side effects of TDD before having the full system implanted. There are two types of screening tests available and the Pain Specialist will determine which test is performed and when required.

Injection method - This procedure consists of a single injection or multiple injections of a small amount of medication into the intrathecal space.

Continuous infusion method - This screening test closely resembles the therapy delivered by the targeted drug pump, and takes place over a few days.

Patients should not undergo a screening test if they have an active infection at the time of the test, have a body too small to accommodate the implanted pump, or if they are allergic to the screening medication.

The *implant procedure* involves a short surgery and generally requires one or two nights in hospital. The implanted pump and catheter are surgically placed under the skin. The surgeon will make an incision and form a pocket to hold the pump (usually in the abdomen), and creates a second incision on the patients back for the catheter. The surgeon will make a small tunnel around the patient's body to connect the catheter to the pump. TDD is a reversible therapy.

As with any surgical procedure, complications can occur and it is important that patients and clinicians discuss any risk prior to accepting therapy.

When in the patient pathway should targeted drug delivery be considered?

In contrast to earlier thinking on the order of treatments in the patient pathway¹⁰, it has been proposed the device therapies be considered at an earlier stage.¹¹

Benefits of TDD include^{12,13}

- Pain relief for patients who have not received adequate relief with conventional therapies, including adequate dose levels of a range of analgesic drugs
- May reduce adverse effects from oral opioids such as nausea, vomiting, sedation, and constipation
- May decrease or eliminate use of oral analgesics
- Increased ability to perform activities of daily living
- Patient control of medication within physician-set limits
- May be effective for patients who do not experience relief from neurostimulation therapy

What are the adverse effects of TDD?

- Technical failure of the pump or catheter may result in sudden loss of pain relief and possible "withdrawal response". Pumps have a "diagnostic port" that allows injection of the content and imaging but other investigations may be needed
- Long term TDD may result in progressive tolerance to administered opioid drugs leading to the need to increase dose (just as occurs with oral therapy). High opioid doses may result in severe side effects such as hormonal change, fluid retention, blood electrolyte abnormalities, paradoxical increases in pain and/ or sudden withdrawal syndrome and other serious drug side effects

Which specialists in Australia offer TDD?

More than 50 pain management centres across Australia provide interventional pain management options to people with chronic pain. Generally, a targeted drug delivery procedure is performed by a Pain Specialist and/or Neurosurgeon.

Multidisciplinary pain clinics have been established in many of Australia's leading hospitals, accepting referrals from pain centres and general practitioners. These clinics can provide a thorough overview of all treatment options available.

Long term TDD requires that patients have access to a team with appropriate knowledge and skills that permit safe and effective use of TDD.

- 1,2 Brogan SE. Intrathecal Therapy for the Management of Cancer Pain. *Curr Pain Headache Rep.* 2006;10: 254-259
- 3 Gerber HR. Intrathecal morphine for chronic benign pain. *Best Pract Res Clin Anaesthesiol.* 2003;17: 429-442
- 4 Nance P, Meythaler J. Intrathecal drug therapy. *Phys Med Rehabil Clin N Am.* 1999;10:385-401, viii-ix
- 5 Ruan X. Drug-related side effects of long-term intrathecal morphine therapy. *Pain Physician.* 2007;10: 357-366.
- 6 Smith TJ, Swainey C, Coyne PJ. Pain management including intrathecal pumps. *Curr Pain Headache Rep.* 2005;9: 243-248
- 7 Winkelmuller M, Winkelmuller W. Long-term effects of continuous intrathecal opioid treatment of chronic pain of nonmalignant etiology. *J Neurosurg.* 1996;85: 458-467
- 8 Medtronic data on file
- 9 Deer TR, Smith HS, Cousins M, et al. Noncancer pain for intrathecal drug delivery. *Pain Physician.* 2010;13:E175-E213
- 10 Krames ES. Intraspinal Opioid Therapy for Nonmalignant Pain: Current Practices and Clinical Guidelines. *J Pain Symptom Manage* 1996;11:333-352
- 11 Stamatatos JM, et al. Live Your Life Pain Free, October 2005. Based on the interventional pain management experience of Dr. John Stamatatos.
- 12 Lamer TJ. *Mayo Clin Proc.* May 1994;69(5):473-80
- 13 Paice JA. Intraspinal morphine for chronic pain: a retrospective, multicenter study. *J Pain Symptom Manage.* 1996;11:71-80