PHARMACY PROCEDURE

Uridine Triacetate for Patients with Early-Onset Severe Toxicities Following 5-Fluorouracil or Capecitabine

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1.0 Introduction

Uridine triacetate is an oral medicine used to treat people at risk of serious toxicity or overdose following administration of 5-fluorouracil and capecitabine. The medicine is usually given within 96 hours of treatment with either 5-fluorouracil or capecitabine and works by inhibiting cell death and damage caused by these medicines. Uridine triacetate is approved by the Food and Drug Administration (FDA) authority in the United States of America (USA) for treatment of serious toxicity or overdose following administration of 5-fluorouracil or capecitabine. However, the treatment is not licensed in either the United Kingdom (UK) or the European Union. As of 2019, there is an agreed supply of the medicine into England intended for use in this indication.

It is common for people receiving either 5-fluorouracil or capecitabine to experience side effects. Most people experience minor side effects (e.g. fatigue, diarrhoea, nausea, loss of appetite) and these can usually be managed at home with supportive medicines. However, some people receiving treatment with 5-fluorouracil or capecitabine will experience more severe side effects which require hospital admission and, in some situations, can be life threatening. The side effects include: myelosuppression, severe diarrhoea, severe mucositis, severe nausea or vomiting, severe skin reactions. It is estimated that between 10-30% of people receiving these drugs experience severe side effects (Henricks et al, 2018; Cancer Research UK, 2020), however, not all patients will require treatment with uridine triacetate. Consensus estimates that around 50 patients per annum in England could be eligible for treatment with uridine triacetate as per the criteria set out by NHS England. Current treatments for people experiencing severe side effects following 5-fluorouracil or capecitabine administration are aimed at lessening or treating the side effects of these medicines, referred to as supportive care which may include but is not limited to:

- Intravenous hydration and intravenous administration of nutrition (parenteral nutrition)
- Antibiotic treatment
- Blood or platelet transfusion
- Medication to increase white cell counts (growth factor treatment)

2.0 Inclusion Criteria

The following criteria must be met for patients exhibiting early onset, severe or life threatening adverse events:

1. Severe or life-threatening adverse events must occur following the end of fluorouracil infusion or most recent administration of capecitabine;
2. Patients must be on their first cycle of treatment with either fluorouracil or capecitabine; and
3. Adverse events must be deemed severe/life threatening by a clinician experienced in fluoropyrimidine prescribing.

Adverse events indicating treatment with uridine triacetate should be graded Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4 and occur in combination. These include, but are not limited to:

- Grade 3 mucositis
- Grade 3 palmar-plantar erythema
- Grade 3 diarrhoea
- Grade 3 myelosuppression.

In rare cases, uridine triacetate may be prescribed in the event of a known overdose or pump malfunction where severe or life-threatening adverse events are likely.

3.0 Exclusion Criteria

1. Non-emergency treatment of adverse reactions associated with fluoropyrimidine chemotherapy
2. Treatment should not commence any earlier than 3 hours after administration of the dose of the fluoropyrimidine chemotherapy
3. Severe or life-threatening adverse events occurring >96 hours following the end of fluorouracil infusion or most recent administration of capecitabine
4. Patients not on their first cycle of treatment with either fluorouracil or capecitabine.

4.0 Dose

Adults: 10g orally every 6 hours for 20 doses.

Treatment with uridine triacetate must be given within 96 hours of development of toxicity or within 96 hours of known overdose as defined above.

5.0 Administration guidance:

Mix each dose with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt and ingest within 30 minutes. Do not chew the granules. Drink at least 100ml of water. If a patient vomits within 2 hours of taking a dose, initiate another complete dose as soon as possible after the vomiting episode. Administer the next dose at the regularly scheduled time. If a patient misses a dose at the scheduled time, administer that dose as soon as possible. Administer the next dose at the regularly scheduled time.

Administer via a nasogastric or gastrostomy tube if necessary. Follow the instructions below to administer a dose by a nasogastric or gastrostomy tube:

1. Prepare approximately 100 mL of a food starch-based thickening product in water and stir briskly until the thickener has dissolved.
2. Crush the contents of one full 10 gram packet of granules to a fine powder.
3. Add the crushed granules to approx 100 mL of the reconstituted food starch-based thickening product.
4. After administration of the mixture, flush the tube with water.

6.0 Procurement Information

Uridine triacetate is a high-cost medicine and is commissioned by NHS England via the Blue-teq registration system.

WEP Clinical are the preferred supplier of uridine triacetate (Vistogard®) in the UK. To place an order the contact number is 0207 887 2235. This medicine is not

licensed for use in Europe or the UK, and prescribing physician will need to complete a request form to complete the order.

7.0 References:

CancerResearchUk.org. (2020). DPD deficiency. Cancer Research UK. [online] Available at: https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/chemotherapy/side-effects/dpd-deficiency [Accessed January 2020].

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Clinical Commissioning Urgent Policy Statement: Uridine triacetate for the treatment of patients exhibiting early onset severe toxicities following 5-fluorouracil or capecitabine administration (all ages) [URN: 1929] Published by NHS England March 2020.

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