

Online Supplementary Material

Costs of Adverse Event Management Associated with First-Line Cetuximab or Panitumumab in Metastatic Colorectal Cancer Patients in Saudi Arabia. *JHEOR*. 2025;12(1):106-112. [doi:10.36469/jheor.2025.130878](https://doi.org/10.36469/jheor.2025.130878)

Table S1: Probability of Severe Adverse Event in Model

Table S2: Model Adverse Events Management Protocols

Table S3: Model Unit Costs

Table S4: OWSA Results of Saudi Payer Perspective Model

Table S1: Probability of Severe Adverse Event in Model

Figure S1: Saudi Payer Perspective Base-Case: All Grade Adverse Events Results

Figure S2: All-Grade Adverse Events OWSA Results of Saudi Payer Perspective Model

This supplementary material has been provided by the authors to give readers additional information about their work.



Table S1. Probability of Severe Adverse Event in Model

Probability of Severe Adverse Event	Cetuximab	Panitumumab	Source
Blood and lymphatic system disorders	41.8%	94.4%	Estimated from meta-analysis study ¹³
Cardiovascular diseases	100.0%	100.0%	
Gastrointestinal disorders	23.9%	19.2%	
General disorders and administration site conditions	21.6%	32.7%	
Metabolism and nutrition disorders	18.1%	22.7%	
Skin disorders	18.9%	22.6%	
Eye disorders	25.1%	31.2%	
Hepatobiliary disorders	25.1%	31.2%	Assumed to be the average of all reported severe grade 3 and 4 AEs reported in meta-analysis study ¹³
Immune system disorders	25.1%	31.2%	
Infections and infestations	25.1%	31.2%	
Musculoskeletal and connective tissue disorders	25.1%	31.2%	
Nervous system disorders	25.1%	31.2%	
Renal and urinary disorders	25.1%	31.2%	
Respiratory, thoracic and mediastinal disorders	25.1%	31.2%	

Table S2. Model Adverse Events Management Protocols

Adverse Events	Management Protocol
Metabolism and nutrition disorders	
Hypokalemia	IV potassium chloride 40 mEq administered slowly Continuous cardiac monitoring - ICU unit monitoring Nutrition support monitoring of blood potassium levels Electrocardiogram
Hypomagnesemia	1 day to adjust level Mg Supplement for 3 months
Hypocalcemia	IV Calcium Calcium supplement for 3 months Vitamin D supplement for 3 months Magnesium supplement for 3 months Nutrition visit Calcium serum level every 3 months over 6 months
Hyperglycemia	Two n Days (to adjust insulin level) <u>Then insulin for 2 months duration:</u> 1- Initiate basal insulin (e.g., insulin glargine) at 0.2 units/kg/day (for 65 Kg patient is 13 units), adjusted based on blood glucose levels. 2- Add prandial insulin (e.g., insulin lispro) at 6 units before meals, adjusted based on pre-meal blood glucose levels. Nutritionist Follow-up every 4 weeks for 2 months
Hypophosphatemia	1 daycare to adjust level
Dehydration (caused by diarrhea or mucositis)	Loperamide - 4 mg orally every 3 hours for 2 days Nutritionist once IV Fluids once (hospital day care) Octreotide - 2mg for 7 days "Total of 20ml Injection"

Adverse Events	Management Protocol
Anorexia	Nutritionist every 4 weeks for 2 months Psychologist Support every 4 weeks for two months Megestrol acetate (400 mg/day) for 2 months Dexamethasone (4 mg/day) - 2 weeks Ondansetron (4-8 mg every 8 hours) - 5 days
Weight loss	Nutritionist every 4 weeks for 2 months Psychologist support every 4 weeks for two months Megestrol acetate (400 mg/day) for 2 months Dexamethasone (4 mg/day) - 2 weeks Albumin and electrolyte level analysis every 3 months for one year
Skin disorders	
Rash acneiform	Urea cream 10% (for 10-14 days), skin examination by dermatologist, hydrocortisone cream 1% (for 10-14 days), clindamycin cream 2% (for 10-14 days), ciprofloxacin 500mg twice daily for 2 weeks, skin care cream for at least 14 days
Itch	Topical corticosteroids Antihistaminic Drug once daily for 2 weeks Liver function analysis Dermatologist Visit
Flaking	Moisturizers (Panthenol) Sun protection cream Topical corticosteroids Dermatologist
Erythema	Topical corticosteroids Calamine lotion Panthenol cream Sun block Dermatologist
Dryness of the skin	Hydrocortisone cream 1% Emollient cream both twice daily for 2 weeks Dermatologist
Skin fissures	Panthenol Topical analgesics Betadine solution Dermatologist
Acne	Topical sebostatic, comedolytic benzoyl peroxide Oral antibiotic - 300 mg of oral clindamycin taken two to three times daily for 5 days Dermatologist
Alopecia	Scalp cooling sessions - 10 sessions Minoxidil solution Dermatologist
Complications in wound healing	Dermatologist Amoxicillin/clavulanic acid 1 g /12hr- for 7 days Betadine solution Wound dressings Paracetamol
Exfoliative dermatitis	Oral antihistaminic once a day for 2 months Panthenol cream or solution Topical corticosteroids Paracetamol 1g/8hrs for 7 days Sunblock cream Systemic corticosteroids (prednisolone tablets 25mg twice daily for 2 months) Dermatologist

Adverse Events	Management Protocol
Dermatitis	Antihistaminic once a day for 2 months Panthenol cream or solution Topical corticosteroids Paracetamol 1gm/8hrs for 7 days Sunblock cream Dermatologist
Discoloration of the skin	Dermatologist Suncream Panthenol Topical hydroquinone
Palmoplantar erythrodysesthesia	Dermatologist Panthenol Paracetamol 1g/8hrs for 7 days Topical corticosteroid cream Vitamin B6 supplementation for 3 months
Cutaneous ulcer	Dressings Topical anesthetics BENZOCAINE (CLOVAINE) Paracetamol 1g/8hrs for 7 days Betadine Solution Dermatologist
Urticaria (mild or moderate reaction related to infusion)	Antihistaminic once a day for 2 months Systematic corticosteroids (25mg twice a day for 2 months) (Oxygen therapy + Vital sign monitoring) = Hospital Day care Dermatologist visit
Wounds	Panthenol Topical analgesics Betadine solution Dressings Amoxicillin/clavulanic acid 1g/12hrs for 7 days Dermatologist
Hypertrichosis	Laser hair removal session Psychologist visit every 4 weeks for 2 months Dermatologist visit
Onychoclasia and nail diseases	Urea cream 10% (for 10-14 days), skin examination by dermatologist, hydrocortisone cream 1% (for 10-14 days), clindamycin cream 2% (for 10-14 days), 300 mg of oral clindamycin taken 2-3 times daily for 5 days, skin care cream for at least 14 days
Hyperhidrosis	Botulinum Toxin Injections two injections in one year Neurologist Twice Lontophoresis sessions
Infections and infestations	
Paronychia	Topical antibiotic Mupirocin Calcium (Bactroban Ointment 2%) Amoxicillin/clavulanic acid 1 g/12hrs for 7 days Paracetamol 1g/8hrs for 7 days Dermatologist
Pustular rash	Dermatologist Topical antibiotics Topical corticosteroids Betadine Solution Amoxicillin/clavulanic acid 1 g/12hrs for 7 days Antihistamine once a day for one month
Cellulite	Dermatologist Nutritionist Panthenol

Adverse Events	Management Protocol
	ILser session Oral clindamycin 300mg/6hrs 10 days
Urinary tract infections	Urologist Amoxicillin/clavulanic acid 1 gm/12hrs for 14 days Urine analysis and urine culture Ibuprofen 600mg/8hrs for 7 days Cranberry supplement 1200 mg/day for 3 months
Folliculitis	Benzoyl peroxide solution Topical clindamycin Topical corticosteroids Oral clindamycin 300mg/6hrs 10 days Oral fluconazole 150 mg once weekly for 4 weeks Dermatologist
Localized infection	Topical mupirocin Oral clindamycin 300mg/6hrs 10 days IV vancomycin 15-20 mg/kg per dose, administered every 8-12 hours for 7 days Paracetamol 1gm/8hrs for 7 days Physician visit
Blood and lymphatic system disorders	
Anemia	Iron supplement for 2 months Epoetin alfa: 40,000 units once weekly for 2 months Monitor hemoglobin levels every 1-2 weeks initially Blood Transfusion Vitamin B12 injection once weekly
Leukopenia	Amoxicillin/clavulanic acid for 7 days Ciprofloxacin for 7 days 3 vials filgrastim
Nervous system disorders	
Migraine	Metoclopramide (dopamine receptor antagonist) 3 times per day for 7 days Sumatriptan 100mg twice for 3 days Neurologist visit
Dizziness	Otolaryngologist, neurologist, or vestibular visits for diagnosis Meclozine, pyridoxine (vitamin B6) once daily for 4 weeks
Insomnia	Melatonin once a day for 3 weeks Psychological support visits every 4 weeks for 3 months
Anxiety	Psychological support visit every 4 weeks for 6 months Escitalopram for 6 months - selective serotonin reuptake inhibitor (SSRI)
Eye disorders	
Conjunctivitis	Systan eye drops for 6 months - 1 bottle/month Ophthalmologist Oral antihistamine for 2 weeks Prednisolone for 2 weeks Antihistamine eye drops
Blepharitis	Amoxicillin/clavulanic acid 1 g/12hrs for 7 days Ophthalmologist visit Systane Ultra for 6 months - 1 bottle/month Corticosteroids for 7 days
Excessive growth of eyelashes	Systane Drops for 6 months - 1 bottle/month Ophthalmologist visit Laser sessions
Hyperlacrimation	Systane eye drops for 6 months - 1 bottle/month Antihistaminic eye drops for 7 days Ophthalmologist visit

Adverse Events	Management Protocol
Ocular hyperemia	Systane eye drops Antihistaminic eye drops Anti-inflammatory eye drops (Acular) Topical vasoconstrictor (Riazolin) Ophthalmologist visit
Xerophthalmia	Systane eye drops Omega-3 fatty acids - twice per day for 3 months Ciclosporin eye drops Ophthalmologist visit
Ocular itching	Systane eye drops for 6 months Antihistaminic eye drops Anti-inflammatory eye drops (Acular) Omega 3 fatty acids twice for 3 months Ophthalmologist visit
Irritation of the eyes	Systane eye drops - 6 months Antihistaminic eye drops Omega 3 fatty acids - twice for 3 months Ophthalmologist visit
Cardiovascular diseases	
Tachycardia	Concor 2.5mg once daily for 3 months Diltiazem Hydrochloride (Dilzem Retard) 60 mg twice daily for 3 months ECG and cardiologist visit every 3 months Electrolyte analysis
Hypertension	Valsartan angiotensin II receptor blocker (ARB) once daily for 1 year/ model horizon Cardiologist every 3 months Electrolyte analysis
Hypotension	Midodrine 2.5mg twice daily for 6 months Cardiologist
Venous thromboembolism	Enoxaparin sodium Clexane 80mg\0.8ml Prefilled Syringe (1 mg/kg subcutaneously every 12 hours for 7 days) Heparin Infusion (18 units/kg/hour (or 12 units/kg/hour) for 7 days Alteplase [thrombolytic agent] 90 mg over 2 hours, with the remainder of the total dose (usually 90 mg) given over the next 24 hours.
Deep vein thrombosis	Enoxaparin sodium (Clexane 80mg\0.8ml Prefilled Syringe; 1 mg/kg subcutaneously every 12 hours for 7 days) Heparin Infusion (18 units/kg/hour or 12 units/kg/hour for 7 days) Alteplase [thrombolytic agent] 90 mg over 2 hours, with the remainder of the total dose (usually 90 mg) given over the next 24 hours.
Arterial thromboembolism	Heparin Infusion (18 units/kg/hour or 12 units/kg/hour) for 7 days Alteplase [thrombolytic agent] 90 mg over 2 hours, with the remainder of the total dose (usually 90 mg) given over the next 24 hours. Aspirin once daily for 3 months Thrombectomy surgery
Hemorrhage	Platelet transfusion Red blood cell Transfusion Intravenous Fluids and Supportive Care/Hospital Day Care Hematologic consultant
Flushes	Venlafaxine (SNRIs): 150 mg/day for 6 months Gabapentin anticonvulsant medication 400mg once for 1 month Acupuncture Psychologist Support every 4 weeks for 6 months
Respiratory, thoracic and mediastinal disorders	

Adverse Events	Management Protocol
Dyspnea	Oxygen therapy Inhaled ipratropium - bronchodilators Budesonide (Pulmicort Flexhaler) - corticosteroid Furosemide injection - Loop diuretic Nutritionist Pulmonologist Visit
Rhinitis	Antihistamines (Claritin) for 7 days Nasal corticosteroids Budesonide Rhinocort Aqua 64mcg spray Nasal decongestant sprays like oxymetazoline (Vicks Sinex nasal spray) Saline nasal spray 15 ml Montelukast - leukotriene receptor antagonists (LTRAs) once daily for 12 weeks (3 months) Physician visit
Epistaxis	Nasal decongestant sprays like oxymetazoline Saline nasal spray 15 ml Topical antibiotic ointment (Mupirocin Calcium) Vitamin K and iron supplements once daily for 2 months Physician visit
Cough	Dextromethorphan (Cough Suppressant) Guaifenesin (Expectorants) Nasal saline irrigation Antihistamines like cetirizine or loratadine once daily for 7 days Nasal corticosteroids Budesonide Rhinocort Aqua 64mcg nasal spray Physician visit
Pulmonary hemorrhage	Oxygen Therapy Blood Transfusion Electrolyte transfusion - IV Fluids = Hospital Day care Antifibrinolytic (Tranexamic Acid) - Administer 10 mg/kg actual body weight 3 to 4 times daily for 8 days Platelet Transfusions Pulmonologist Interventional Radiologist: for procedures like bronchial artery embolization
Hemoptysis	Antifibrinolytic Agents: Tranexamic Acid 10 mg/kg actual body weight 3 to 4 times daily for 8 days Platelet transfusion Bronchoscopy Follow-Up Imaging: Chest X-rays or CT scans Pulmonologist
Pulmonary embolism	Oxygen Therapy Paracetamol 1g/8hrs for 7 days Enoxaparin sodium/Clexane 80mg/0.8ml Prefilled Syringe (1 mg/kg subcutaneously every 12 hours) Antifibrinolytic Agents: Tranexamic Acid 10 mg/kg actual body weight 3 to 4 times daily for 8 days Surgical embolectomy Inferior vena cava filter Follow-up every month with cardiothoracic surgeons
Hypoxia	Oxygen Therapy Antibiotics: For bacterial infections Amoxicillin/clavulanic acid 1g twice daily for 7 days pulse oximetry and Arterial Blood Gases (ABGs) follow up Enoxaparin sodium/Clexane 80mg/0.8ml Prefilled Syringe (1 mg/kg subcutaneously every 12 hours)

Adverse Events	Management Protocol
	Corticosteroids (prednisolone 25 mg for 2 weeks) Chest CT Scans Pulmonologist
Dysphonia	Steroids prednisolone 25 mg for 2 weeks Paracetamol 1gm/8hours for 7 days Physician visit
Gastrointestinal disorders	
Diarrhea	Loperamide 4 mg: 2 times daily for maximum 3 days
Constipation	Lactulose syrup twice daily for 10 days Hospital Care Day
Nausea and vomit	Granisetron iv once then tablet twice daily for 2 days Hospital Day Care
Abdominal pain	Paracetamol Nausea and Vomiting treatment (Primperan) - Metoclopramide 10 mg - 3 times/day for 3 months CT scans or ultrasound Physician visit
Stomatitis	1-2 days hospital admission Oral antibiotic (ciprofloxacin+flagyl) for 7 days Oral steroids (prednisolone) for 1 week Antifungal therapy (nystatin) from 7-10 days Mouth wash (1 week)
Rectal hemorrhage	CBC Tranexamic acid 1 g 3 times daily for two weeks Proton Pump Inhibitors (PPIs):Omeprazole 20-40 mg orally once daily for 8 weeks Octreotide Acetate (Sandostatin 0.1mg-ml Amp) ampoule Endoscopic Therapy (endoclips) Nutritionist, oncologists, gastroenterologists, and interventional radiologists visits
Xerostomia	Dentist Visit Saliva substitutes as biotene oral products - twice a day for 3 months Cevimeline 30 mg taken three times a day for three months
Dyspepsia	Omeprazole 20-40 mg orally once daily for 8 weeks H2 Receptor Antagonists: Famotidine: 20-40 mg orally twice daily, duration: 6-8 weeks Magnesium Hydroxide/Aluminum Hydroxide: 10-20 mL or 1-2 tablets as needed for symptom relief Prokinetic Agents: Metoclopramide: 10 mg orally three times daily before meals and at bedtime for 3 weeks Cytoprotective Agents: Sucralfate 1 gram orally four times daily, duration: Typically used for 4-8 weeks Follow-up Gastroenterologist and nutritionist
Cheilitis	Hydrocortisone 1% Cream 2 to 3 times for two weeks Topical antibacterial: Mupirocin 2% Ointment: Apply to the affected area 2-3 times daily for 7-10 days Emollients and Moisturizers: Petroleum Jelly (Vaseline) Topical Calcineurin Inhibitors: Tacrolimus (Protopic 0.1% Ointment) 2 times for 4 weeks Systemic Treatments (for severe cases): Oral Steroids (e.g., Prednisone 40mg for 2 weeks) Regular physician visit
Reflux disease	Omeprazole: 20-40 mg orally once daily for 8 weeks Famotidine: 20-40 mg orally twice daily for 6-8 weeks Magnesium Hydroxide/Aluminum Hydroxide: 10-20 mL or 1-2 tablets as needed for symptom relief Prokinetic Agents: Metoclopramide: 10 mg orally three times daily before meals and at

Adverse Events	Management Protocol
	bedtime for 3 weeks Follow-up Gastroenterologist and nutritionist - one visit for two months
Gastrointestinal perforation	Intravenous Fluids: Immediate IV fluid resuscitation to manage hypovolemia and shock- One day hospital care Empirical antibiotic therapy to prevent or treat sepsis. Piperacillin-Tazobactam: 3.375 to 4.5 g IV every 6-8 hours for 7 to 10 days Exploratory Laparotomy Repair of the Perforation GIT CT Scan Nutrition Support
Intestinal obstruction	Metoclopramide: 10 mg orally three times daily before meals and at bedtime for 3 weeks Paracetamol 1gm/8 hrs for 7 days Antispasmodics: Hyoscyamine 0.125mg 3 times/day for one week Stool Softeners/Laxatives: 40 to 150 mg docusate sodium orally divided in 1 to 4 doses for one week. Steroids: dexamethasone 25mg for two weeks Octreotide - 2mg for 7 days Nutritional Support every month for 6 months Nasogastric Tube (NGT) Placement Fluid and Electrolyte Replacement Bowel Resection: Removing the obstructed portion of the intestine GIT Physician: Follow-up every month for 6 months
Rectovaginal fistulas	Amoxicillin/clavulanic acid 1g/12 hours for 7 days Stool Softeners/Laxatives: 40 to 150 mg docusate sodium orally divided in 1 to 4 doses for one week Infliximab: 3 mg/kg IV at 0, 2, and 6 weeks, then q8Weeks thereafter for three months Octreotide - 2mg for 7 days Surgical Treatment: Fistulotomy
Proctalgia	Ibuprofen 600mg/8 hrs for 7 days Anesthetic cream Topical corticosteroids Anticonvulsants: gabapentin 400mg once daily for 1 month
Hepatobiliary disorders	
Increased liver enzyme levels (AST, ALT, AP)	Hepatoprotective Agents: ursodeoxycholic acid (UDCA) [900 mg/day for 3 month] Antioxidants: Supplements such as N-acetylcysteine (NAC)/acetylcysteine can help reduce oxidative stress on the liver: one injection Prednisolone 25mg for two weeks to decrease inflammation Regular Monitoring: Frequent liver function tests to monitor enzyme levels and assess liver function every month for 3 months Hepatologist Visit
Renal and urinary disorders	
Proteinuria	Angiotensin II Receptor Blockers (ARBs): Valsartan [40 mg once daily for 3 months] can reduce proteinuria Diuretics: Furosemide IV for 7 days Corticosteroids: In cases of severe proteinuria or nephrotic syndrome, prednisone 25mg for 2 weeks Nephrologist Visit
Musculoskeletal and connective tissue disorders	
Arthralgia	Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Voltaren Emulgel Prednisolone 25mg once for 2 weeks duloxetine 60mg once daily for one month gabapentin 400 mg once daily for one month

Adverse Events	Management Protocol
	Acupuncture Physiotherapy sessions Orthopedic physician visit
Myalgia	Muscle Relaxants (Cyclobenzaprine Hydrochloride 5mg twice daily) for one month Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Prednisolone 25mg once for 2 weeks Duloxetine 60mg once daily for one month Gabapentin 200 mg once daily for one month Topical analgesics Acupuncture Physiotherapy sessions Orthopedic Physician visit
Fistula	Infliximab loading dose of 5 mg/kg body weight is given intravenously at weeks 0, 2, and 6 then every 8 weeks, with a dose of 5 mg/kg body weight for one year Octreotide - 2mg for 7 days Fistulotomy
Muscle weakness	Cyclobenzaprine Hydrochloride 5mg twice daily Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Physical Therapy psychological support every 4 weeks for 3 months
Back pain	Cyclobenzaprine Hydrochloride 5mg twice daily for one month Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Prednisolone 25mg once for 2 weeks Duloxetine 60mg once daily for one month Gabapentin 200 mg once daily for one month Topical analgesics Acupuncture Physiotherapy sessions Orthopedic physician visit
Dorsal pain	Cyclobenzaprine Hydrochloride 5mg twice daily for one month Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Prednisolone 25mg once for 2 weeks duloxetine 60mg once daily for one month gabapentin 200 mg once daily for one month Topical analgesics Acupuncture Physiotherapy sessions Orthopedic physician visit
Pain in the extremities	Cyclobenzaprine Hydrochloride 5mg twice daily for one month Ibuprofen 600mg/8hrs for 7 days Paracetamol 1g/8hrs for 7 days Prednisolone 25mg once for 2 weeks Duloxetine 60mg once daily for one month Gabapentin 200 mg once daily for one month Topical analgesics Acupuncture Physiotherapy sessions Orthopedic Physician visit
Reproductive system and breast disorders	
Ovarian failure	Goserelin 3.6 mg monthly for one year

Adverse Events	Management Protocol
	Hormone Replacement Therapy Medroxyprogesterone Acetate (Provera) Dosage: 2.5-10 mg daily for 10 days Ovarian Tissue Cryopreservation Gynecologist Visit
Pelvic pain	Physical Therapy Psychological Therapy Acupuncture Ibuprofen 600 mg every 8 hours for 7 days Tramadol for 7 days Antidepressants: Duloxetine 60 mg daily
General disorders and administration site conditions	
Mucositis	1-2 days hospital admission Oral antibiotic (ciprofloxacin+flagyl) for 7 days Oral steroids (prednisolone) for 1 week Antifungal therapy (nystatin) from 7-10 days Mouth wash (1 week)
Anaphylactic shock (serious reaction related to infusion)	Epinephrine: 0.3-0.5 mg IM once Diphenhydramine: 25-50 mg IV/IM once Methylprednisolone: 1-2 mg/kg IV, followed by a oral corticosteroids over 7 days. Beta-2 Agonists - Salbutamol Ventolin Respiratory Solution/Albuterol: 2.5-5 mg via nebulizer, as needed for bronchospasm. IV Fluids: 1-2 liters rapid infusion - Hospital Day Care
Bronchospasm (serious reaction related to infusion)	Beta-2 Agonists Drug: Salbutamol Anticholinergics Drug: Ipratropium Systemic Corticosteroids Drugs: Methylprednisolone Injection then Prednisone 40-60 mg orally for 7 days Norepinephrine Bitartrate: 0.3-0.5 mg IM Magnesium Sulfate: 1-2 grams IV over 20 minutes. Continuous monitoring of vital signs, oxygen saturation, and respiratory status. Reassessment after each treatment intervention and need for further treatment. Observation for at least 4-6 hours after the resolution of acute symptoms to monitor for recurrence.
Ache	Physical Therapy Psychological Therapy Acupuncture Ibuprofen 600 mg every 8 hours for 7 days Morphine 10-30 mg every 4 hours as needed for pain. Antidepressants: Duloxetine 60 mg daily for one month Anticonvulsants: Gabapentin 300-600 mg three times daily for one month Topical Agents Lidocaine Steroids: Prednisone 25 mg daily for two weeks
Fatigue and asthenia	Stimulants: Methylphenidate: 5-10 mg three times, up to 60 mg/day for 3 months Duloxetine: 30-60 mg daily for 3 months Prednisone: 25 mg daily for two weeks Physiotherapy Psychotherapy
Fatigue	Methylphenidate 5-10 mg three times, up to 60 mg/day for 3 months Duloxetine: 30-60 mg daily for 3 months Prednisone: 25 mg daily for two weeks Physiotherapy Psychotherapy
Pyrexia	Acetaminophen: 1000 mg every 6 hours for 7 days Ibuprofen: 600 mg every 8 hours for 7 days Piperacillin-Tazobactam: 3.375-4.5 grams IV every 6-8 hours 14 days.

Adverse Events	Management Protocol
	Prednisone: 25 mg daily for 2 weeks Oral or intravenous fluids as needed - Hospital Day Care Antibiotic Culture
Peripheral edema	Furosemide: 40 mg orally once daily for 5 days Prednisone: 25 mg daily for 2 weeks Albumin: 25% solution, 50-100 mL IV over 30-60 minutes. Compression stockings Physical Therapy
Lethargy	Methylphenidate: 5-10 mg three times, up to 60 mg/day for 3 months Duloxetine: 30-60 mg daily for 3 months Prednisone: 25 mg daily for two weeks Physiotherapy Psychotherapy
Chills	Acetaminophen: 1000 mg/6 hours for 7 days. Ibuprofen: 600 mg every 8hours for 7 days Piperacillin-Tazobactam: 3.375-4.5 grams IV every 6-8 hours for 14 days Prednisone: 25 mg daily for 2 weeks Loratadine: 10 mg daily for 10 days - chills are associated with allergic reactions to treatment
Immune system disorders	
Hypersensitivity	Hospital Day Care Hydrocortisone 100 mg IV Antihistaminic (diphenhydramine 50 mg IV) Bronchodilator

Table S3. Model Unit Costs

Item	Base-Case	Lower Limit	Higher Limit
Medications			
IV Potassium Chloride, Injection 20meq	SAR 0.80	SAR 0.64	SAR 0.96
Intravenous calcium (calcium gluconate), 10 ml	SAR 0.75	SAR 0.60	SAR 0.90
Calcium Supplement (1500mg) Tablet	SAR 0.05	SAR 0.04	SAR 0.06
Vitamin d supplement 50,000 units capsule	SAR 3.64	SAR 2.91	SAR 4.37
Magnesium supplement (mg oxide 400 mg) tablet	SAR 0.07	SAR 0.06	SAR 0.08
Insulin Glargine 300u/ML - 1.5 ML Injection (1unit Cost)	SAR 0.09	SAR 0.08	SAR 0.11
Insulin Lispro (ASPART) - 100u/ML - 3 ML Injection (1unit Cost)	SAR 0.09	SAR 0.07	SAR 0.11
Loperamide 2mg Tablet	SAR 0.89	SAR 0.71	SAR 1.07
Octreotide 0.1mg/ML 1 ML Injection	SAR 32.20	SAR 25.76	SAR 38.64
Iv fluids for dehydration (ns)	SAR 4.50	SAR 3.60	SAR 5.40
Vancomycin - 500mg Vial - Cost Per 1mg	SAR 0.01	SAR 0.01	SAR 0.01
Megestrol Acetate 40mg Tablet	SAR 1.00	SAR 0.80	SAR 1.20
Dexamethasone 4 mg tablet	SAR 0.84	SAR 0.67	SAR 1.01
Claritine-antihistamine 10 mg tablet	SAR 0.02	SAR 0.02	SAR 0.02
Betamethasone dipropionate cream	SAR 11.00	SAR 8.80	SAR 13.20
Dexpanthenol ointment	SAR 11.85	SAR 9.48	SAR 14.22
Sun block cream - average public price	SAR 90.00	SAR 72.00	SAR 108.00
Calamine lotion	SAR 1.50	SAR 1.20	SAR 1.80
Voltarene emulgel	SAR 1.90	SAR 1.52	SAR 2.28
Betadine solution	SAR 83.97	SAR 67.18	SAR 100.76
Benzoyl peroxide gel	SAR 4.70	SAR 3.76	SAR 5.64
Clindamycin 300mg Capsule	SAR 1.75	SAR 1.40	SAR 2.10
Minoxidil topical solution	SAR 67.65	SAR 54.12	SAR 81.18
Amoxicillin/clavulanic acid 625 mg tablet	SAR 0.27	SAR 0.22	SAR 0.32
Paracetamol 500 mg tablet	SAR 0.02	SAR 0.02	SAR 0.02
Prednisolone 25 mg tablet	SAR 0.71	SAR 0.57	SAR 0.85
Hydroquinone cream	SAR 3.00	SAR 2.40	SAR 3.60
Vitamin b6 supplement 40 mg tablet	SAR 0.10	SAR 0.08	SAR 0.12
Benzocaine (clovaine) gel	SAR 18.80	SAR 15.04	SAR 22.56
Botulinum toxin 100 iu injection	SAR 775.00	SAR 620.00	SAR 930.00
Mupirocin calcium (bactroban ointment)	SAR 20.60	SAR 16.48	SAR 24.72
Fuscidin ointment	SAR 1.63	SAR 1.30	SAR 1.96
Cranberry Supplement 750mg Tablet	SAR 3.17	SAR 2.53	SAR 3.80
Ibuprofen 600 mg tablet	SAR 0.52	SAR 0.42	SAR 0.63
Benzoyl peroxide gel	SAR 4.70	SAR 3.76	SAR 5.64
Fluconazole 150 mg tablet	SAR 0.90	SAR 0.72	SAR 1.08
Iron supplements 190 mg tablet	SAR 0.06	SAR 0.05	SAR 0.07
Epoetin alfa 1000 units injection	SAR 35.00	SAR 28.00	SAR 42.00
Vitamin b12 sc injection	SAR 3.50	SAR 2.80	SAR 4.20
Metoclopramide 10 mg tablet	SAR 0.20	SAR 0.16	SAR 0.24
Somatriptan 100 mg tablet	SAR 17.36	SAR 13.89	SAR 20.83
Meclozine,pyridoxine (vitamin b6)	SAR 0.50	SAR 0.40	SAR 0.60
Melatonin 3 mg tablet	SAR 2.00	SAR 1.60	SAR 2.40
Escitalopram 10 mg tablet	SAR 1.93	SAR 1.54	SAR 2.32
Systane ultra eye drops	SAR 47.80	SAR 38.24	SAR 57.36
Antihistaminic eye drops (olopatadine) eye drops	SAR 20.00	SAR 16.00	SAR 24.00
Anti-inflammatory eye drops (acular) eye drops	SAR 20.00	SAR 16.00	SAR 24.00
Topical vasoconstrictor (riazolin) eye drops	SAR 16.65	SAR 13.32	SAR 19.98

Item	Base-Case	Lower Limit	Higher Limit
Cyclosporin eye drops	SAR 117.50	SAR 94.00	SAR 141.00
Omega-3 fatty acid capsule	SAR 0.96	SAR 0.77	SAR 1.15
Amiodarone 200mg Tablets	SAR 0.80	SAR 0.64	SAR 0.96
Concor cor 2.5 mg tablet	SAR 0.43	SAR 0.34	SAR 0.52
Diltiazem hydrochloride (dilizem retard) 60 mg tablet	SAR 0.17	SAR 0.14	SAR 0.20
Candesartan 16 mg tablet	SAR 1.13	SAR 0.90	SAR 1.36
Valsatan Tablet - 160mg	SAR 1.20	SAR 0.96	SAR 1.44
Midodrine 2.5 mg tablet	SAR 2.26	SAR 1.81	SAR 2.71
Enoxaparin Sodium 40 Mg SC Prefilled Syringe-1mg Price	SAR 0.40	SAR 0.32	SAR 0.48
Heparin IV 5000units/ML - 5ml - 1 Unit Price	SAR 0.004	SAR 0.00	SAR 0.00
Alteplase (actilyse) - 50 Mg IV Injection - 1mg Price	SAR 31.34	SAR 25.07	SAR 37.61
Aspirin 81 mg tablet	SAR 0.07	SAR 0.06	SAR 0.08
Venlafaxine 150 mg capsule	SAR 1.21	SAR 0.97	SAR 1.45
Gabapentin 400mg Capsule	SAR 2.20	SAR 1.76	SAR 2.64
Ipratropium inhalation	SAR 70.00	SAR 56.00	SAR 84.00
Budesonide (pulmicort flexhaler) - inhalation	SAR 164.00	SAR 131.20	SAR 196.80
Furosemide 10mg/ML - 25ml Solution for Injection	SAR 20.00	SAR 16.00	SAR 24.00
Furosemide 40mf Tablet	SAR 1.01	SAR 0.81	SAR 1.21
Budesonide (rhinocort aqua) - nasal spray	SAR 50.65	SAR 40.52	SAR 60.78
Oxymetazoline - (xylometazoline) - nasal spray	SAR 1.00	SAR 0.80	SAR 1.20
Saline nasal spray	SAR 2.00	SAR 1.60	SAR 2.40
Montelukast - 10mg Tablet	SAR 0.17	SAR 0.14	SAR 0.20
Vitamin K Supplement 10mg Tablet	SAR 0.20	SAR 0.16	SAR 0.24
Dextromethorphan syrup	SAR 8.25	SAR 6.60	SAR 9.90
Guaifensin syrup	SAR 6.50	SAR 5.20	SAR 7.80
Loratadine 10mg Tablet	SAR 0.02	SAR 0.02	SAR 0.02
Tranexamic Acid - 500mg/ml Injection - 1mg Price	SAR 0.01	SAR 0.01	SAR 0.01
Cevimeline tablet	SAR 32.70	SAR 26.16	SAR 39.24
Saliva substitutes - packet (1 use) (caphosol)	SAR 15.00	SAR 12.00	SAR 18.00
Omeprazole 20mg Tablet	SAR 0.50	SAR 0.40	SAR 0.60
Famotidine 20mg Injection	SAR 7.10	SAR 5.68	SAR 8.52
Magnesium Hydroxide 200mg Tablet	SAR 0.07	SAR 0.06	SAR 0.08
Sucralfalte 1gm Tablet	SAR 1.10	SAR 0.88	SAR 1.32
Hydrocortisone cream	SAR 1.90	SAR 1.52	SAR 2.28
Vaseline cream tube	SAR 2.50	SAR 2.00	SAR 3.00
Tacrolimus 0.1% cream	SAR 188.80	SAR 151.04	SAR 226.56
Piperacillin/Tazobactam 4gm Vial	SAR 14.30	SAR 11.44	SAR 17.16
Tazobactam,ceftolozane vial	SAR 3,282.10	SAR 2,625.68	SAR 3,938.52
Hyoscyamine (levsin tab 0.125mg) tablet	SAR 0.39	SAR 0.31	SAR 0.47
Docusate sodium, sennosides (laxatrol) FCT 50mg/8.6 mg	SAR 0.39	SAR 0.31	SAR 0.47
Infliximab 100mg Vial - Price Per 1mg	SAR 8.14	SAR 6.51	SAR 9.77
Ursodeoxycholic Acid 250mg Tablet	SAR 2.25	SAR 1.80	SAR 2.70
Acetylcysteine 10ml Injection	SAR 7.60	SAR 6.08	SAR 9.12
Tramadol 50mg Tablet	SAR 0.32	SAR 0.26	SAR 0.38
Duloxetine 30mg Tablet	SAR 2.30	SAR 1.84	SAR 2.76
Cyclobenzaprine hydrochloride 5mg capsule	SAR 1.04	SAR 0.83	SAR 1.24
Goserelin (zoladex depot) 3.6mg sc injection	SAR 550.00	SAR 440.00	SAR 660.00
Medroxyprogesterone Acetate 5mg Tablet	SAR 1.37	SAR 1.10	SAR 1.64
Morphine 30mg Tablet	SAR 1.50	SAR 1.20	SAR 1.80
Lidocaine hydrochloride ointment	SAR 49.00	SAR 39.20	SAR 58.80
Diphenhydramine 1ml Injection	SAR 3.23	SAR 2.58	SAR 3.88
Chlorphenamine Injection 10mg/ml Ampoule	SAR 1.21	SAR 0.97	SAR 1.45

Item	Base-Case	Lower Limit	Higher Limit
Salbutamol (ventolin) respiratory solution	SAR 6.90	SAR 5.52	SAR 8.28
Norepinephrine bitartrate 4ml Ampoule	SAR 4.80	SAR 3.84	SAR 5.76
Magnesium Sulfate 5ml Injection	SAR 1.50	SAR 1.20	SAR 1.80
Methylphenidate solution for injection	SAR 30.35	SAR 24.28	SAR 36.42
Albumin human solution for infusion	SAR 208.70	SAR 166.96	SAR 250.44
Skin care cream	SAR 20.00	SAR 16.00	SAR 24.00
Ciprofloxacin 500mg Tablets	SAR 0.30	SAR 0.24	SAR 0.36
Amoxicillin/Clavulanic Acid 1gm Tablets	SAR 0.52	SAR 0.42	SAR 0.62
Prednisolone tablets	SAR 0.35	SAR 0.28	SAR 0.42
Nystatin drops	SAR 2.40	SAR 1.92	SAR 2.88
Flagyl tablets	SAR 0.10	SAR 0.08	SAR 0.12
Mouth wash	SAR 2.00	SAR 1.60	SAR 2.40
Urea cream	SAR 3.50	SAR 2.80	SAR 4.20
Hydrocortisone 1% cream	SAR 1.90	SAR 1.52	SAR 2.28
Clindamycin 2% cream	SAR 4.60	SAR 3.68	SAR 5.52
Loperamide 2mg Tablets	SAR 0.80	SAR 0.64	SAR 0.96
Lactulose syrup	SAR 3.75	SAR 3.00	SAR 4.50
Diphenhydramine 50mg IV	SAR 5.00	SAR 4.00	SAR 6.00
Broncodilator "Breztri"	SAR 190.00	SAR 152.00	SAR 228.00
Hydrocortisone 100mg IV	SAR 3.00	SAR 2.40	SAR 3.60
Ondansetron tablet	SAR 13.80	SAR 11.04	SAR 16.56
Zofran IV	SAR 15.30	SAR 12.24	SAR 18.36
Neupogen Vial / Filgrastim 300mcg PFS	SAR 45.00	SAR 36.00	SAR 54.00
Apixaban 5mg Tablet	SAR 1.50	SAR 1.20	SAR 1.80
Resources			
Nutritionist support - HCP visit	SAR 345.00	SAR 276.00	SAR 414.00
Blood potassium levels	SAR 40.00	SAR 32.00	SAR 48.00
Electrocardiogram	SAR 160.00	SAR 128.00	SAR 192.00
Hospitalization cost	SAR 600.00	SAR 480.00	SAR 720.00
Day care cost	SAR 300.00	SAR 240.00	SAR 360.00
Calcium serum level	SAR 40.00	SAR 32.00	SAR 48.00
Iv session	SAR 100.00	SAR 80.00	SAR 120.00
Psychologist support - HCP visit	SAR 345.00	SAR 276.00	SAR 414.00
Albumin analysis	SAR 40.00	SAR 32.00	SAR 48.00
Complete electrolyte level analysis	SAR 950.00	SAR 760.00	SAR 1,140.00
Liver function test	SAR 248.00	SAR 198.40	SAR 297.60
Dermatologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Wound dressings	SAR 3.60	SAR 2.88	SAR 4.32
Oxygen therapy session	SAR 200.00	SAR 160.00	SAR 240.00
Dermal laser session average	SAR 450.00	SAR 360.00	SAR 540.00
Neurologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Subcutaneous injection	SAR 100.00	SAR 80.00	SAR 120.00
Urologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Urine analysis	SAR 180.00	SAR 144.00	SAR 216.00
Urine culture	SAR 180.00	SAR 144.00	SAR 216.00
General practitioner visit	SAR 345.00	SAR 276.00	SAR 414.00
Hemoglobin level test	SAR 250.00	SAR 200.00	SAR 300.00
Complete blood count	SAR 147.00	SAR 117.60	SAR 176.40
Ent physician visit	SAR 345.00	SAR 276.00	SAR 414.00
Ophthalmologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Cardiologist	SAR 345.00	SAR 276.00	SAR 414.00
Thrombectomy surgery average	SAR 8,750.00	SAR 7,000.00	SAR 10,500.00

Item	Base-Case	Lower Limit	Higher Limit
Platelet transfusion	SAR 3,100.00	SAR 2,480.00	SAR 3,720.00
Packed RBCS transfusion	SAR 1,500.00	SAR 1,200.00	SAR 1,800.00
Intravenous infusion	SAR 100.00	SAR 80.00	SAR 120.00
Hematologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Acupuncture	SAR 135.00	SAR 108.00	SAR 162.00
Pulmonologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Bronchial artery embolization	SAR 11,000.00	SAR 8,800.00	SAR 13,200.00
Interventional radiologist	SAR 345.00	SAR 276.00	SAR 414.00
Bronchoscopy	SAR 2,500.00	SAR 2,000.00	SAR 3,000.00
Chest x-ray	SAR 155.00	SAR 124.00	SAR 186.00
Chest CT scan	SAR 1,035.00	SAR 828.00	SAR 1,242.00
Surgical embolectomy average	SAR 8,750.00	SAR 7,000.00	SAR 10,500.00
Inferior vena cava filter	SAR 5,000.00	SAR 4,000.00	SAR 6,000.00
Cardiothoracic surgeon visit	SAR 345.00	SAR 276.00	SAR 414.00
Arterial blood gases measure	SAR 100.00	SAR 80.00	SAR 120.00
Oncologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Gastrologist	SAR 345.00	SAR 276.00	SAR 414.00
Dentist visit	SAR 250.00	SAR 200.00	SAR 300.00
Exploratory laparotomy	SAR 35,000.00	SAR 28,000.00	SAR 42,000.00
Git repair of the perforation surgery	SAR 6,000.00	SAR 4,800.00	SAR 7,200.00
Git CT scan	SAR 1,035.00	SAR 828.00	SAR 1,242.00
Nasogastric tube placement	SAR 250.00	SAR 200.00	SAR 300.00
Bowel resection surgery: removing the obstructed portion of the intestine	SAR 21,000.00	SAR 16,800.00	SAR 25,200.00
Hepatologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Physiotherapy session	SAR 250.00	SAR 200.00	SAR 300.00
Orthopedic visit	SAR 345.00	SAR 276.00	SAR 414.00
Nerve blocks injection of anesthetics or steroids near specific nerves	SAR 8,500.00	SAR 6,800.00	SAR 10,200.00
Allergy testing and desensitization	SAR 800.00	SAR 640.00	SAR 960.00
Gynecologist visit	SAR 345.00	SAR 276.00	SAR 414.00
Bacterial culture and sensitivity test	SAR 200.00	SAR 160.00	SAR 240.00
Compression stockings	SAR 112.00	SAR 89.60	SAR 134.40
Vestibular Function Test	SAR 520.00	SAR 416.00	SAR 624.00
Endoscopic Surgery for Endoclips placement	SAR 9,504.00	SAR 7,603.20	SAR 11,404.80
Productivity costs			
Average working days in Saudi Arabia - week	5.00	4.00	6.00
Average working days in Saudi Arabia - month	22	17.39	26.09
Saudi patient average wages / day	SAR 437.66	SAR 350.13	SAR 525.20

Table S4. OWSA Results of Saudi Payer Perspective Model

Adverse Event Costs	All Grade Adverse Events		
	Cetuximab	Panitumumab	Difference
Adverse events costs (Minimum)	SAR 651,439	SAR 3,034,242	SAR 2,382,803
Adverse events costs (Median)	SAR 3,582,917	SAR 16,688,331	SAR 13,105,415
Adverse events costs (Maximum)	SAR 6,514,394	SAR 30,342,421	SAR 23,828,027

Figure S1. Saudi Payer Perspective Base-Case: All Grade Adverse Events Results

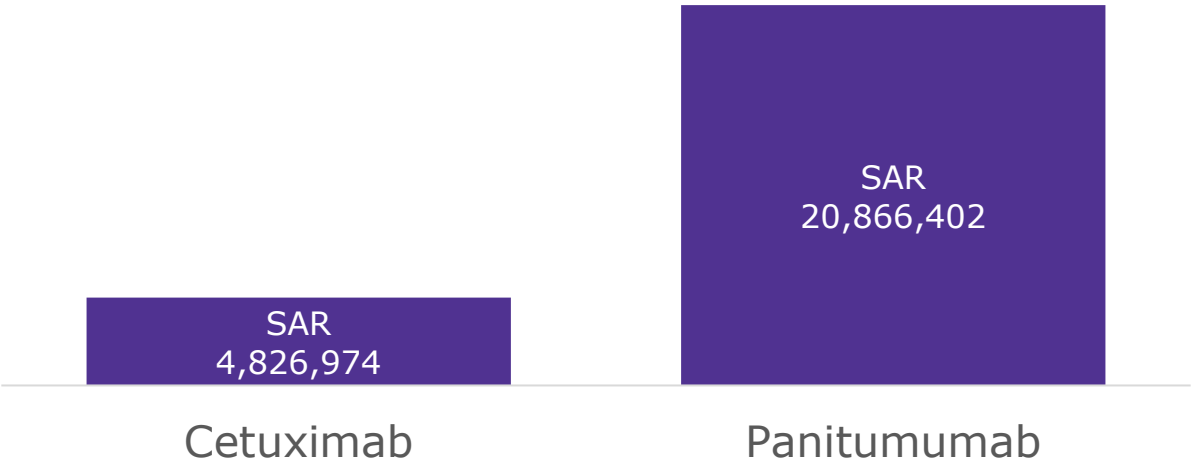


Figure S2. All-Grade Adverse Events OWSA Results of Saudi Payer Perspective Model

